EXHIBIT M

PI: **BenMohamed, Lbachir**	Title: Developing a Multi-epitope Pan-Coronavirus Vaccine	
Received: 05/22/2020	FOA: PAR20-178 Clinical Trial:Not Allowed	Council: 08/2020
Competition ID: FORMS-E	FOA Title: Emergency Awards: Rapid Investigation of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and Coronavirus Disease 2019 (COVID-19) (R01 Clinical Trial Not Allowed)	
1 R01 AI158060-01	Dual:	Accession Number: 4440589
IPF: 577504	Organization: UNIVERSITY OF CALIFORNIA-IRVINE	
Former Number:	Department: Ophthalmology/Cell.Mol.Immunol	
IRG/SRG: ZAI1 JHM-X (S3)	AIDS: N	Expedited: N
Subtotal Direct Costs (excludes consortium F&A) Year 1: 499,999 Year 2: 499,999 Year 3: 499,999 Year 4: 499,999 Year 5: 499,999	[redacted] Humans: Y Clinical Trial: N Current HS Code: 30 HESC: N HFT: N Special Topics: Research related to Coronavirus Disease 2019 (COVID-19)	New Investigator: N Early Stage Investigator: N

Senior/Key Personnel:	*Organization:*	*Role Category:*
LBACHIR BENMOHAMED	The Regents of the University of California, Irvine	PD/PI
MICHAEL BUCHMEIER	The Regents of the University of California, Irvine	Co-Investigator
DONALD FORTHAL	The Regents of the University of California, Irvine	Co-Investigator
SEBASTIAN SCHUBL	The Regents of the University of California, Irvine	Co-Investigator
ANTHONY NESBURN	The Regents of the University of California, Irvine	Co-Investigator
CHRISTINE MCLAREN	The Regents of the University of California, Irvine	Co-Investigator
JAMES JESTER	The Regents of the University of California, Irvine	Other (Specify)-Other Significant Contributor
ERIC PEARLMAN	The Regents of the University of California, Irvine	Other (Specify)-Other Significant Contributor
LANNY HSIEH	The Regents of the University of California, Irvine	Other (Specify)-Other Significant Contributor
Peter Burkhard	Sunomix Therapeutics	Other (Specify)-Consortium PI

OMB Number: 4040-0010
Expiration Date: 12/31/2022

APPLICATION FOR FEDERAL ASSISTANCE
SF 424 (R&R)

3. DATE RECEIVED BY STATE	**State Application Identifier**

1. TYPE OF SUBMISSION*

❍ Pre-application ● Application ❍ Changed/Corrected Application

4.a. Federal Identifier

b. Agency Routing Number

c. Previous Grants.gov Tracking Number

2. DATE SUBMITTED 2020-05-22

Application Identifier

5. APPLICANT INFORMATION

Organizational DUNS*: 046705849

Legal Name*: The Regents of the University of California, Irvine
Department:
Division:
Street1*: 141 Innovation Drive, Suite 250
Street2:
City*: Irvine
County: Orange
State*: CA: California
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 92697-7600

Person to be contacted on matters involving this application
Prefix: First Name*: Jasmin Middle Name: Last Name*: Ramirez Suffix:
Position/Title: CONTRACT & GRANT OFFICER
Street1*: 141 Innovation, Suite 250
Street2:
City*: Irvine
County: Orange
State*: CA: California
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 92697-7600
Phone Number*: 9498242460 Fax Number: 9498242094 Email: jasminjr@uci.edu

6. EMPLOYER IDENTIFICATION NUMBER *(EIN) or (TIN)** 1-952226406-A1

7. TYPE OF APPLICANT* H: Public/State Controlled Institution of Higher Education

Other (Specify):
Small Business Organization Type ❍ Women Owned ❍ Socially and Economically Disadvantaged

8. TYPE OF APPLICATION*

● New ❍ Resubmission
❍ Renewal ❍ Continuation ❍ Revision

If Revision, mark appropriate box(es).

❍ A. Increase Award ❍ B. Decrease Award ❍ C. Increase Duration
❍ D. Decrease Duration ❍ E. Other *(specify)* :

Is this application being submitted to other agencies?* ❍Yes ●No What other Agencies?

9. NAME OF FEDERAL AGENCY*
National Institutes of Health

10. CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBER
TITLE:

11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT*
Developing a Multi-epitope Pan-Coronavirus Vaccine

12. PROPOSED PROJECT
Start Date* 09/01/2020
Ending Date* 08/31/2025

13. CONGRESSIONAL DISTRICTS OF APPLICANT
CA-045

SF 424 (R&R) APPLICATION FOR FEDERAL ASSISTANCE

14. PROJECT DIRECTOR/PRINCIPAL INVESTIGATOR CONTACT INFORMATION

Prefix: First Name*: LBACHIR Middle Name: Last Name*: BENMOHAMED Suffix:
Position/Title: Professor/Director
Organization Name*: The Regents of the University of California, Irvine
Department: Ophthalmology/Cell.Mol.Immunol
Division: SCHOOL OF MEDICINE
Street1*: Hewitt Hall Room 2032
Street2:
City*: Irvine
County: Orange
State*: CA: California
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 92697-7600
Phone Number*: (949) 824-8937 Fax Number: (949) 824-9626 Email*: lbenmoha@uci.edu

15. ESTIMATED PROJECT FUNDING

a. Total Federal Funds Requested*	$3,831,570.00
b. Total Non-Federal Funds*	$0.00
c. Total Federal & Non-Federal Funds*	$3,831,570.00
d. Estimated Program Income*	$0.00

16.IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?*

a. YES ○ THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON:
DATE:

b. NO ● PROGRAM IS NOT COVERED BY E.O. 12372; OR
○ PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW

17. By signing this application, I certify (1) to the statements contained in the list of certifications* and (2) that the statements herein are true, complete and accurate to the best of my knowledge. I also provide the required assurances * and agree to comply with any resulting terms if I accept an award. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. (U.S. Code, Title 18, Section 1001)

● I agree*

** The list of certifications and assurances, or an Internet site where you may obtain this list, is contained in the announcement or agency specific instructions.*

18. SFLLL or OTHER EXPLANATORY DOCUMENTATION File Name:

19. AUTHORIZED REPRESENTATIVE

Prefix: First Name*: Jasmin Middle Name: Last Name*: Ramirez Suffix:
Position/Title*: CONTRACT & GRANT OFFICER
Organization Name*: The Regents of the University of California, Irvine
Department:
Division:
Street1*: 141 Innovation, Suite 250
Street2:
City*: Irvine
County: Orange
State*: CA: California
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 92697-7600
Phone Number*: 9498242460 Fax Number: 9498242094 Email*: jasminjr@uci.edu

Signature of Authorized Representative*
Jasmin Ramirez

Date Signed*
05/22/2020

20. PRE-APPLICATION File Name:

21. COVER LETTER ATTACHMENT File Name:CoverLetter1013860953.pdf

424 R&R and PHS-398 Specific

Table Of Contents

Project/Performance Site Location(s)

Project/Performance Site Primary Location

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name:	The Regents of the University of California Irvine
Duns Number:	046705849
Street1*:	843 Health Sciences Road
Street2:	Hewitt Hall , Building 843, 2nd Floor, Room 2032
City*:	Irvine
County:	Orange
State*:	CA: California
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	92697-7600
Project/Performance Site Congressional District*:	CA-045

Project/Performance Site Location 1

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name:	Sunomix Therapeutics
DUNS Number:	080437688
Street1*:	7625 Heatherly LN
Street2:	
City*:	San Diego
County:	
State*:	CA: California
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	92130-5602
Project/Performance Site Congressional District*:	CA-052

Additional Location(s) File Name:

OMB Number: 4040-0010
Expiration Date: 12/31/2022

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* ● **Yes** ○ **No**

1.a. If YES to Human Subjects

Is the Project Exempt from Federal regulations? ● Yes ○ No

If YES, check appropriate exemption number: — 1 — 2 — 3 ✔ 4 — 5 — 6 — 7 — 8

If NO, is the IRB review Pending? ○ **Yes** ○ **No**

IRB Approval Date:

Human Subject Assurance Number 00004071

[redacted]

3. Is proprietary/privileged information included in the application?* ○ **Yes** ● **No**

4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* ○ **Yes** ● **No**

4.b. If yes, please explain:

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? ○ Yes ○ No

4.d. If yes, please explain:

5. Is the research performance site designated, or eligible to be designated, as a historic place?* ○ **Yes** ● **No**

5.a. If yes, please explain:

6. Does this project involve activities outside the United States or partnership with international collaborators?* ○ **Yes** ● **No**

6.a. If yes, identify countries:

6.b. Optional Explanation:

	Filename
7. Project Summary/Abstract*	Abstract1013860950.pdf
8. Project Narrative*	ProjectNarrative1013860951.pdf
9. Bibliography & References Cited	LiteratureCited1013860952.pdf
10.Facilities & Other Resources	Facilities_COVID1013860980.pdf
11.Equipment	Equipment_COVIDv21013860982.pdf

Tracking Number: GRANT13114391
Funding Opportunity Number: PAR-20-178. Received Date: 2020-05-22T18:02:25.000-04:00

SUMMARY

Humanity is confronting a pandemic caused by the new Corona Virus 2 (SARS-CoV-2) infection. **Our long-term goal** is to develop a potent prophylactic pan-Coronavirus vaccine to stop/reduce past, current and future Coronavirus infections and/or diseases. While SARS-CoV-2-induced antibody and $CD4^+$ and $CD8^+$ T cell responses are critical to reducing viral infection in the majority of asymptomatic individuals, an excessive proinflammatory cytokine storm appears to lead to acute respiratory distress syndrome in many symptomatic individuals. **Major gaps**: Identifying the epitope specificities, the phenotype and function of B cells, $CD4^+$ T cells and $CD8^+$ T cells associated with "natural protection seen in asymptomatic individuals (those who are infected, but never develop any major symptoms) should guide the development of a future coronavirus vaccine. **Preliminary Results**: [redacted]

PROJECT NARRATIVE

The WHO and US authorities have declared the recent outbreak of SARS-CoV-2, which causes COVID-19, a public health emergency. In this proposal, we leverage and extend our multi-epitope SAPN-based vaccine approach to COVID-19. We will design, produce, and preclinically test the multi-epitope pan-Coronavirus vaccine candidates (designated as Pan-CoV vaccines), delivered mucosally using our SAPN vaccine delivery platform.

FACILITIES AND OTHER RESOURCES

Lab:
The PI has a total of approximately 1200 sq. ft. of well-equipped lab space in the Dept. of Ophthalmology located in The Laboratory of Cellular and Molecular Immunology of The Gavin Herbert Eye Institute (GHEI). The lab consists of all necessary equipment for the proposed project with the exception of high end equipment which is shared amongst the investigators at GHEI.

Clinics: Univ. of California Irvine Medical Center houses a GCRC facility. The PI has an approved facility to drow and use blood from HSV infected animal visiting UCI medical center clinics. Since this project involves using blood and saliva from COVID-19 patients, specific COVID-19 IRB, IBC and ABSL3 protocols are presently being put in place, and researchers have already taken appropriate ABSL3 training.

Office:
The PI and lab members are linked to the campus ethernet backbone via desktop Pentium computers. Each is equipped with word processing, data and statistical management, desktop publishing and presentation software.

The PI maintains an office in the Dept. of Ophthalmology of approximately 150 sq. ft. adjacent to the lab. six under-graduate students and two technicians have desks and pentium computers available in the lab proper.

EQUIPMENT

The Cellular and Molecular Immunology Laboratory, Gavin Herbert Institute (GHEI), UC Irvine, directed by Dr. BenMohamed has access to state-of-the-art facilities and technical equipment, established infrastructure for technical support and subject recruitment, and collegial environments to support the research as proposed in this application.

Major equipment available include the following: one Aria II 6 color Flow cytometer, one Luminex 100, one Confocal Microscope, a Caliper/Xenogen IVIS-100 imaging system, a Bio-Rad iMark Absorbance Microplate Reader with Microplate Manager 6 software, a Bio-Rad ELISA Microplate washer, and all necessary equipment for tissue culture and tissue staining including: 8 CO_2 and temperature controlled incubators, 4 BL2 Biosafety hoods, 2 chemical hoods, 4 microcentrifuges, 2 vacuum ovens, several temperature controlled water baths, various 4°/-20°C refrigerator/freezers, four -80°C freezers, 4 automated LN2 large capacity cell freezers, 2 high speed centrifuges, 1 cell harvester, 1 ultracentrifuge with rotors, 2 incubator-shaker for bacteria, scintillation counters (in the core facility), and laser imaging system (fluorescent and phosphorimaging)1 dark room with film developer and an enlarger, 2 fluorescence microscopes, 2 inverted microscopes with digital photographic equipment, 1 beta and 1 gamma scintillation counters, DNA sequencing equipment (in the core facility), 1 real time thermal cycler, 1 nucleic acid and protein electrophoresis and transfer. The laboratory is equipped with an Agillent 2100 Bioanalyzer, a Leica Laser Microdissection Station, 2 PCR machines, including real time PCR, 1 hybridization washing station, 2 hybridization ovens, manifolds and platforms for high throughput plasmid isolation and purification and a DNA sequencer.

OMB Number: 4040-0010
Expiration Date: 12/31/2022

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Prefix: First Name*: LBACHIR Middle Name Last Name*: BENMOHAMED Suffix:

Position/Title*:	Professor/Director
Organization Name*:	The Regents of the University of California, Irvine
Department:	Ophthalmology/Cell.Mol.Immunol
Division:	SCHOOL OF MEDICINE
Street1*:	Hewitt Hall Room 2032
Street2:	
City*:	Irvine
County:	Orange
State*:	CA: California
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	92697-7600

Phone Number*: (949) 824-8937 Fax Number: (949) 824-9626

E-Mail*: lbenmoha@uci.edu

Credential, e.g., agency login: Lbenmohamed

Project Role*: PD/PI Other Project Role Category:

Degree Type: Ph.D. Degree Year: 1997

Attach Biographical Sketch*: File Name: BenMohamed_BioSketch_COVID1013860987.pdf

Attach Current & Pending Support: File Name:

Tracking Number: GRANT13114391 Funding Opportunity Number: PAR-20-178 . Received Date: 2020-05-22T18:02:25.000-04:00

PROFILE - Senior/Key Person

Prefix: First Name*: MICHAEL Middle Name Last Name*: BUCHMEIER Suffix:

Position/Title*: Professor
Organization Name*: The Regents of the University of California, Irvine
Department: MOLECULAR BIOLOGY AND BIOCHEMI
Division: AYALA SCHOOL OF BIOLOGICAL SCI
Street1*: 2222 Bio Sci 3, University of
Street2:
City*: Irvine
County: Orange
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 92697-7600

Phone Number*: (949) 824-5781 Fax Number: (949) 824-9437

E-Mail*: m.buchmeier@uci.edu

Credential, e.g., agency login: mjbuchmeier

Project Role*: Co-Investigator Other Project Role Category:

Degree Type: Ph.D. Degree Year: 1976

Attach Biographical Sketch*: File Name: BuchmeierBio1013860979.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: DONALD Middle Name Last Name*: FORTHAL Suffix:

Position/Title*: Professor of Medicine- Infectious Diseases
Organization Name*: The Regents of the University of California, Irvine
Department: INFECTIOUS DISEASES
Division: SCHOOL OF MEDICINE
Street1*: 3044 Hewitt Hall
Street2:
City*: Irvine
County: Orange
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 92697-7600

Phone Number*: (949) 824-3366 Fax Number: (949) 824-5490

E-Mail*: d.forthal@uci.edu

Credential, e.g., agency login:

Project Role*: Co-Investigator Other Project Role Category:

Degree Type: Degree Year:

Attach Biographical Sketch*: File Name: Biosketch_DF1013860955.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: SEBASTIAN Middle Name DOMINIK Last Name*: SCHUBL Suffix:

Position/Title*: HS Associate Clinical Professor
Organization Name*: The Regents of the University of California, Irvine
Department:
Division:
Street1*: 333 City Blvd W, Suite 1600
Street2:
City*: Orange
County: Orange
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 92697-7600

Phone Number*: (714) 509-2121 Fax Number:

E-Mail*: sschubl@uci.edu

Credential, e.g., agency login:

Project Role*: Co-Investigator Other Project Role Category:

Degree Type: MD Degree Year: 2004

Attach Biographical Sketch*: File Name: SchublBio1013860962.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: ANTHONY Middle Name Last Name*: NESBURN Suffix:

Position/Title*: Adjunct Professor/Vice Chair of Research
Organization Name*: The Regents of the University of California, Irvine
Department: Ophthalmology
Division: School of Medicine
Street1*: UCI SOM - Ophthalmology Research
Street2: Hewitt Hall Room 2026
City*: Irvine
County: Orange
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 92697-7600

Phone Number*: (949) 824-6892 Fax Number: (949) 824-9626

E-Mail*: anesburn@uci.edu

Credential, e.g., agency login: anesburn

Project Role*: Co-Investigator Other Project Role Category:

Degree Type: M.D. Degree Year: 1960

Attach Biographical Sketch*: File Name: NesburnBio1013860988.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: CHRISTINE Middle Name Last Name*: MCLAREN Suffix:

Position/Title*: Professor
Organization Name*: The Regents of the University of California, Irvine
Department: GENETIC EPIDEMIOLOGY RESEARCH
Division: School of Medicine
Street1*: Irvine Hall, Room 214
Street2:
City*: Irvine
County: Orange
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 92697-7600

Phone Number*: (949) 824-4007 Fax Number: (949) 824-1343

E-Mail*: cmclaren@uci.edu

Credential, e.g., agency login: cmclaren

Project Role*: Co-Investigator Other Project Role Category:

Degree Type: Ph.D. Degree Year: 1983

Attach Biographical Sketch*: File Name: McLarenBio1013860966.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: JAMES Middle Name Last Name*: JESTER Suffix:

Position/Title*: Professor
Organization Name*: The Regents of the University of California, Irvine
Department: Ophthalmology
Division: SCHOOL OF MEDICINE
Street1*: Hewitt Hall Room 2036
Street2:
City*: Irvine
County: Orange
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 92697-7600

Phone Number*: (949) 824-8047 Fax Number: (949) 824-9626

E-Mail*: jjester@uci.edu

Credential, e.g., agency login: JJESTER

Project Role*: Other (Specify) Other Project Role Category: Other Significant Contributor

Degree Type: Ph.D. Degree Year: 1978

Attach Biographical Sketch*: File Name: JesterBio_v21013784341.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: PROF First Name*: ERIC Middle Name Last Name*: PEARLMAN Suffix:

Position/Title*: Professor/Director
Organization Name*: The Regents of the University of California, Irvine
Department: Ophthalmology/INST FOR IMMUNO
Division: School of Medicine
Street1*: 850 Health Sciences Rd.
Street2: Hewitt Hall
City*: Irvine
County: Orange
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 92697-4375

Phone Number*: (949) 824-1867 Fax Number: (949) 824-2305

E-Mail*: epearlma@uci.edu

Credential, e.g., agency login: EPEARLMAN

Project Role*: Other (Specify) Other Project Role Category: Other Significant Contributor

Degree Type: Ph.D. Degree Year: 1988

Attach Biographical Sketch*: File Name: PearlmanBio1013784342.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: LANNY Middle Name L. Last Name*: HSIEH Suffix:

Position/Title*: HS Associate Professor
Organization Name*: The Regents of the University of California, Irvine
Department: Hospitalist Program
Division:
Street1*: 101 The City Drive
Street2: BLDG 26, Suite 1001, ZOT 4076H
City*: Orange
County: Orange
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 92697-7600

Phone Number*: (714) 456-5429 Fax Number: (714) 456-7182

E-Mail*: llhsieh@uci.edu

Credential, e.g., agency login:

Project Role*: Other (Specify) Other Project Role Category: Other Significant Contributor

Degree Type: MD Degree Year: 1999

Attach Biographical Sketch*: File Name: biosketch_Hsieh1013860956.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: Peter Middle Name Last Name*: Burkhard Suffix:

Position/Title*: Chief Scientific Officer
Organization Name*: Sunomix Therapeutics
Department:
Division:
Street1*: 3210 Merryfield Row
Street2:
City*: San Diego
County:
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 92130-5602

Phone Number*: 858-829-6063 Fax Number: 858-900-5059

E-Mail*: pburkhard@sunomixtherapeutics.com

Credential, e.g., agency login: PETERBURKHARD

Project Role*: Other (Specify) Other Project Role Category: Consortium PI

Degree Type: Ph.D. Degree Year: 1995

Attach Biographical Sketch*: File Name: 2__Burkhard_Bio1013860968.pdf

Attach Current & Pending Support: File Name:

BIOGRAPHICAL SKETCH

NAME: Lbachir BenMohamed

eRA COMMONS USER NAME: Lbenmohamed

POSITION TITLE: **Professor of Immunology**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	COMPLET DATE	FIELD OF STUDY
University Paris VII, Paris, France	B.S.	06/1990	Biochemistry
Pasteur Institute, Paris, France	M.S.	06/1991	Immuno-parasitology
Pasteur Institute & University Paris VII, Paris, France	Ph.D.	03/1997	Immunology
City of Hope National Medical Center, Duarte, CA	Post. Doc.	12/1998	Viral Immunology
Beckman Research Institute of Immunology, CA	Post. Doc.	12/2000	T cell Immunology

A. Personal Statement:

The goals of this R01 grant application entitled *"Developing a Multi-epitope, Pan-Coronavirus Vaccine"* are to design, produce, and preclinically test the multi-epitope pan-Coronavirus vaccine candidates (designated as Pan-CoV vaccines), delivered mucosally using a self-assembling protein nanoparticles (SAPNs) Ag delivery platform.

I am an immunologist and virologist that graduated from Pasteur Institute, Paris, France, with a strong career focus on vaccine development for viruses. I will bring to the project more than 30 years of experience in cellular and molecular immune responses to infectious viral pathogens. I have authored more than 100 peer-reviewed papers on immunology, virology and vaccine development.

For over 20 years, I am the founder and the head of Cellular and Molecular Immunology Laboratory at UC Irvine, which has been working on viral infection, immunity and vaccine development projects. Our team is recognized as a world leader in the fields of herpes T cell immunity, memory T cells and T-cell based herpes vaccines and immunotherapies. We pioneered "asymptomatic" viral epitope mappings for both $CD4^+$ and $CD8^+$ T cells and the identification of inflammasomes pathways associated with inflammatory responses induced by virulent and non-virulent strains of herpes virus in human and animal models.

I have the expertise, leadership, and motivation to successfully carry out the proposed work. I have been the PI on successfully carried out NIH R21, R03 and R01 grant projects. I have worked on cellular and molecular immunology of infectious diseases for over 25 years, beginning as a graduate and post doc at the Pasteur Institute (France). I have devoted more than 20 years to understanding basic mechanisms of epitope mapping, antigen recognition and immune responses, measuring immune activity, and developing disease intervention strategies against many viral infection and disease. I have published over 100 peer-reviewed publications, most in herpes immunology, including papers in *Nature Medicine, The Journal of Virology, The Journal of Immunology, Mucosal Immunology*, *Vaccine, Human Immunology* and *Investigative in Ophthalmology and Visual Sciences.*

For this project, I have gathered a multidisciplinary team of 9 additional top basic scientists and clinicians with complementary expertise required for completion of this vaccine project. These include Dr. Buchmeier brings to the project more than 35 years of experience with the Coronaviruses including SARS-CoV (*see Investigators section*).

B. Positions and Honors:

Positions and Employment:

1998-1999 Post Doc, Dept. of Hematology/Bone Marrow transp., City of Hope Medical Center, CA.
1999-2000 Research Fellow: Dept. of Immunology. Beckman Research Institute, City of Hope, CA,
2001-2002 Scientist. Ophthalmology Research. Cedars-Sinai Medical Center, Los Angeles, CA.
2002-2007 Assistant Professor and Director Cellular Mol. Immunology Laboratory, UC Irvine, Irvine, CA
2007-2014 Associate Professor and Director Cellular Mol. Immunology Laboratory, UC Irvine, Irvine, CA
2014-present Full Professor & Director Cellular & Molecular Immunology Laboratory, UC Irvine, Irvine, CA
2016-present Scientist Immunologist, Sunomix Therapeutics, Inc., San Diego, CA

Other Experience and Professional Memberships:

2010-present NIH Reviewer National Institutes of Health (NIAID, NEI and NCI).
07-2010 NIH Reviewer, Member Conflict: Anterior Eye Disease (AED) Study Section [ZRG1].
02-2011 NIH Reviewer, Anterior Eye Disease (AED) Study Section.
06-2011 NIH Reviewer, NIH SBIR/STTR Grants, Small Business Diagnostic grants.
02-2012 NIH Reviewer, Strategies for the Protection of Pregnant Women (NIAID, ZAI1-BDP-M-M1).
06-2012 NIH Reviewer, Vaccines Against Microbial Diseases (VMD) Study section.
06-2013 NIH Reviewer, NIH Reviewer, Vaccines ZRG1 IMM N12.
10-2013 NIH Reviewer, Vaccine Development and Immunology (ZRG1 IM-V) study section.
11-2013 NIH Reviewer, NIAID-DAIDS-NIH-AI-2012150, Immunology Quality Assessment Program.
02-2014 NIH Reviewer, Ad-hoc reviewer NIAID. Mucosal Environment (ZAI1 RB -A (J1) Study Section.
06-2014 NIH Reviewer, Immunology Study Section (ZRG1 IMM-N12).
02-2015 NIH Reviewer, Diseases and Pathophysiology of the Visual System (DPVS) Study Section.
06-2015 NIH Reviewer, Special Emphasis Panel ZRG1 III-F 08 F, Innate Immunity and Inflammation.
06-2015 NIH Reviewer, Innate Immunity and Inflammation (III) Study Section.
07-2015 NIH Reviewer, Small Business: Non HIV Microbial Vaccines ZRG1 IMM-R(12) Study Section.
10-2015 NIH Reviewer, Immunity and Host Defense Study Section (IHD) Study Section.
02-2016 NIH Reviewer, Cellular and Molecular Immunology (CMIA) Study Section.
03-2016 NIH Reviewer, Special Emphasis Panel ZRG1-BDCN-N-55, Study Section.
05-2016 NIH Reviewer, Special Emphasis Panel ZRG1-BDCN-W-90 Study Section.
06-2016 NIH Reviewer, Cellular and Molecular Immunology (CMIA) Study Section.
02-2017 NIH Reviewer, Ocular Surface, Cornea, Anterior Segment (ZRG1-BDCN-J-81) Study Section.
02-2017 NIH Reviewer, Immunity and Host Defense Study Section (IHD) Study Section.
03-2017 NIH Reviewer, Immunology Study Section (ZRG1-IMM-C-02) Study Section.
06-2017 NIH Reviewer, Innate Immunity and Inflammation (III) Study Section.
10-2017 NIH Reviewer, Clinical Neuroimmunology and Brain Tumors Study Section (CNBT) Study Section.
10-2017 NIH Reviewer, Ocular Surface, Cornea, Anterior Segment (ZRG1-BDCN-J-81) Study Section.
11-2017 NIH Reviewer, Ocular Surface, Cornea, Anterior Segment (ZRG1-BDCN-R-03) Study Section.
03-2018 NIH Reviewer, Special Emphasis Panel ZRG1-BDCN-W-90 Study Section.
04-2018 NIH Reviewer, Member Conflict: Topics in Virology (ZRG1 IDM-W-02) Study Section.
06-2018 NIH Reviewer, Clinical Trials (ZAI1-MFH-M-S2) Study Section.
06-2018 NIH Reviewer, Cellular and Molecular Immunology (CMIA) Study Section.
09-2018 NIH Reviewer, Lung Cellular, Molecular, and Immunobiology (LCMI) Study Section.
11-2018 NIH Reviewer, Sexually transmitted diseases (ZAI1-AWA-M-J1) Study Section.
01-2019 NIH Reviewer, Adjuvant Discovery/Development for Vaccines and for Autoimmune and Allergic Diseases (ZAI1-IMM-J1) Study Section.

Honors:

1992-1996 Fellowship from the French Government, France
1996-1997 Fellowship from Pasteur Institute, Paris, France
1998 Award from American Society of Hematology, USA
1999 Award from American Society of Hematology, USA
2006; Award from Research to Prevent Blindness (RPB), New York, USA
2009, 2010, 2014 and 2018 Award from the Discovery Fund for Eye Research, Los Angeles, CA, USA

C. Contribution to Science:

Dr. BenMohamed's work has been highly influential in shaping the current understanding of herpes T cell-mediated immunity in both humans and [redacted] (**1**) He recently introduced a novel concept of symptomatic/asymptomatic immunology to defined the underlying mechanisms by which T cells specific to asymtomatic epitopes protect against herpes. (**2**) He developed mucosal delivery of clinically approved lipopeptide vaccines and immunotherapies to protect against herpes infection and disease. (**3**) He discovered new immune evasion mechanisms by which HSV-1 LAT gene interferes with T cell immunity. (**4**) He developed a novel "[redacted] 6255 model of genital herpes (a model used in this proposal). (**5**) Finally, his lab has identified many HSV-1 and HSV-2 human $CD4^+$ and $CD8^+$ T cell epitopes for vaccine and immunotherapy purposes.

These five major contributions to science are detailed below:

1. Discovered a novel "*asymptomatic memory $CD8^+$ T cells concept*" in herpes virus immunity: Generation and maintenance of high quantity and quality memory $CD8^+$ T cells determine the level of protection from viral, bacterial, and parasitic re-infections, and hence constitutes a primary goal for T cell epitope-based human vaccines and immunotherapeutics. Dr. BenMohamed recently introduced a new direction in developing T cell-based human herpes vaccines and immunotherapeutics based on the emerging new concept of "*asymptomatic memory $CD8^+$ T cells*". For this he categorized the phenotype, the function and the anatomical locations of two new major distinct sub-populations of memory symptomatic and asymptomatic HSV-specific $CD8^+$ T cells based on their protective vs. pathogenic function. Several asymptomatic HSV human epitopes have been since identified in Dr. BenMohamed's laboratory and are currently considered for T cell-based human herpes "asymptomatic" vaccine.

a. Up-Regulation of Multiple $CD8^+$ T Cell Exhaustion Pathways is Associated to Recurrent Herpes Simplex Virus Type 1 Infection. Pierre-Grégoire Coulon; Soumyabrata Roy; Swayam Prakash; Ruchi Srivastava; Nisha Dhanushkodi; Stephanie Salazar; Cassandra Amezquita; Lan Nguyen; Hawa Vahed; Angela M. Nguyen; Wasay R. Warsi; Caitlin Ye; Edgar A. Carlos-Cruz; Uyen T. Mai & **BenMohamed L.** *The Journal of Immunology*. **2020**. *In Press*.
b. Phenotypic and Functional Signatures of Herpes Simplex Virus-Specific Effector Memory $CD73^+CD45RA^{high}CCR7^{low}CD8^+$ T_{EMRA} and $CD73^+CD45RA^{low}CCR7^{low}CD8^+$ T_{EM} Cells Are Associated with Asymptomatic Herpes. Srivastava; R. Coulon P.G., Roy, S.; Chilukuri S.; Garg S. & **BenMohamed L.** *The Journal of Immunology*. **2018**. 201(8):2315-2330. **PMID: 30201808.**
c. HLA-A02:01-Restricted Epitopes Identified from the Herpes Simplex Virus Tegument Protein VP11/12 Preferentially Recall Polyfunctional Effector Memory $CD8^+$ T Cells from Seropositive Asymptomatic Individuals and Protect "Humanized" HLA-A*02:01 Transgenic Mice Against Herpes. Srivastava; R. Khan A.A., Nesburn, A.B.; Wechsler S.L. & **BenMohamed L.** *The Journal of Immunology*. **2015**. 194(5): 2232-48. **PMID: 25617474.**
d. Phenotypic and Functional Characterization of Herpes Simplex Virus Glycoprotein B Epitope-specific Effector and Memory $CD8^+$ T Cells from Ocular Herpes Symptomatic and Asymptomatic Individuals. Arif Azam Khan; Ruchi Srivastava; Doran Spencer; Daniel Fremgen; Hawa Vahed; Patricia P. Lopes; Thanh T Pham; Charlie Hewett; Jasmine Kuang; Nicolas Ong; Lei Huang; Vanessa M. Scarfone, Anthony B. Nesburn; Steven L. Wechsler & **BenMohamed L.** *The Journal of Virology*. **2015**. 89(7): 3776-92. **PMID: 25609800.**

2. Developed mucosal delivery of clinically approved vaccines to protect against herpes simplex virus: Targeting of the genital mucosal immune system with subunit vaccines has failed to induce potent and durable local $CD8^+$ T cell immunity, which is crucial for protection. Dr. BenMohamed is the key developer and co-inventor of a new promising vaccine strategy that uses mucosal delivery of clinically approved lipopeptide vaccine molecules, laser adjuvant vaccine, and recently prime/pull vaccine strategy. Many researchers have now successfully tested these vaccine strategies, around the world, to protect against many infectious mucosal pathogens.

a. CXCL17 Chemokine–Dependent Mobilization of CXCR8+ CD8+ Effector Memory and Tissue-Resident Memory T Cells in the Vaginal Mucosa Is Associated with Protection against Genital Herpes. Srivastava, R., Hernandez-Ruiz, M., Khan, A.A. Fouladi, M.A., Kim, G.J., Ly, V.T., Yamada,

T., Lam, C., A. Sarain, S.A., Boldbaatar, U., Zlotnik, A., Bahraoui, E. & **BenMohamed L**. *The Journal of Immunology*. **2018**. **PMID: 29438765**.

b. Laser Adjuvant-Assisted Peptide Vaccine Promotes Skin Mobilization of Dendritic Cells and Enhances Protective $CD8^+$ T_{EM} and T_{RM} Cell Responses Against Herpes Infection and Disease. Lopes PP, Todorov G, Pham TT, Nesburn AB, Bahraoui E, & **BenMohamed L**. *The Journal of Virology*. **2018**. **PMID: 29437979**.

c. [redacted]

d. A genital tract peptide epitope vaccine targeting TLR-2 efficiently induces local and systemic CD8+ T cells and protects against herpes simplex virus challenge. Zhang X, Chentoufi AA, Dasgupta G, Nesburn AB, Wu M, Zhu X, Carpenter D, Wechsler SL, You S, & **BenMohamed L.** *Mucosal Immunology*. (*Nature Publishing Group*). **2009.** 2(2):129-43. **PMID: 19129756**.

3. Discovered exhaustion as a novel immune evasion mechanism of HSV-specific $CD8^+$ T cells, a mechanism that is induced by herpes LAT gene expressed during herpes virus latency: We demonstrated, for the first time, in both [redacted] model of herpes infection that most of the HSV-1-specific $CD8^+$ T cells that are selectively retained in sensory ganglia, the site of latent infection, were phenotypically and functionally exhausted. In this novel immune evasion mechanisms, HSV-1 LAT gene promotes functional exhaustion (i.e., dysfunction) of HSV-specific $CD8^+$ T cells resulting in virus reactivation.

a. [redacted]

b.

c. The Herpes Simplex Virus-1 Encoded Latency-Associated Transcript Promotes Dysfunctional Virus-Specific $CD8^+$ T Cells in Latently Infected Trigeminal Ganglia: A Novel Immune Evasion Mechanism. Chentoufi, A.A., E. Kritzer, M. Tran, G. Dasgupta, R. EA., J. Xianzhi, D. Carpenter, O. Osorio, A. B. Nesburn, L. Wechsler & **BenMohamed, L**. *The Journal of Virology*. **2011**. 85(17): 9127-38. **PMID: 21715478.**

d. The herpes simplex virus type 1 latency-associated transcript can protect neuron-derived C1300 and Neuro2A cells from granzyme B-induced apoptosis and CD8 T-cell killing. Jiang X^1, Chentoufi AA, Hsiang C, Carpenter D, Osorio N, **BenMohamed L**, Fraser NW, Jones C, Wechsler SL. *The Journal of Virology*. **2011**. 85(5): 2325-32. **PMID: 21177822.**

4. Developed "humanized" Human Leukocyte Antigen 6255 **model of recurrent herpes virus infection:** The choice of the right [redacted] that reliably reflects recurrent herpes infection and disease, as occurs in humans, is crucial in determining the underlying immune mechanisms that control recurrent herpes. We recently developed an a "humanized" HLA Tg [redacted] for UV-B induced recurrent herpetic corneal disease.

a. [redacted]

b. [redacted]

c. [redacted]

d. A Novel Human Leukocyte Antigen (HLA-A*0201) Transgenic Rabbit Model to Evaluate the Protective Efficacy of Human CD8+ T-Cell Epitopes against Ocular Herpes Infection and Disease. Chentoufi A.A., Dasgupta G., Azeem A. Choudhury Z., Christensen N, Wechsler SL., Nesburn AB & **BenMohamed L**. *The Journal of Immunology*. **2010**. 184(5): 2561-71. **PMID: 20124097.**

5. Leader in mapping of human CD4$^+$ and CD8$^+$ T cell epitopes from HSV-1 protein antigens for genital herpes vaccine and immunotherapy purposes: Dr. BenMohamed's efforts in last 2 decades had let to identification of several CD4$^+$ and CD8$^+$ T cell epitopes from many herpes glycoprotein and tegument proteins that are currently being considered fro clinical herpes vaccine trials.

a. HLA-A02:01-restricted epitopes identified from the herpes simplex virus tegument protein VP11/12 preferentially recall polyfunctional effector memory CD8+ T cells from seropositive asymptomatic individuals and [redacted] against ocular herpes. Srivastava R, Khan AA, Spencer D, Vahed H, Lopes PP, Thai NT, Wang C, Pham TT, Huang J, Scarfone VM, Nesburn AB, Wechsler SL. & **BenMohamed L**. *The Journal of Immunology*. **2015**. 194(5): 2232-48. **PMID: 25617474**.

b. Asymptomatic HLA-A*02:01-restricted epitopes from herpes simplex virus glycoprotein B preferentially recall polyfunctional CD8+ T cells from seropositive asymptomatic individuals and protect [redacted] against ocular herpes. Dervillez X1, Qureshi H, Chentoufi AA, Khan AA, Kritzer E, Yu DC, Diaz OR, Gottimukkala C, Kalantari M, Villacres MC, Scarfone VM, McKinney DM, Sidney J, Sette A, Nesburn AB, Wechsler SL. & **BenMohamed L**. *The Journal of Immunology*. **2013**. 191(10): 5124-38. **PMID: 24101547**.

c. HLA-A*0201-restricted CD8+ cytotoxic T lymphocyte epitopes identified from herpes simplex virus glycoprotein D. Chentoufi AA, Zhang X, Lamberth K, Dasgupta G, Bettahi I, Nguyen A, Wu M, Zhu X, Mohebbi A, Buus S, Wechsler SL, Nesburn AB. & **BenMohamed L**. *The Journal of Immunology*. **2008**. 180(1): 426-437. **PMID: 18097044**.

d. Asymptomatic human CD4+ cytotoxic T-cell epitopes identified from herpes simplex virus glycoprotein B. Chentoufi AA, Binder NR, Berka N, Durand G, Nguyen A, Bettahi I, Maillère B., & **BenMohamed, L**. *The Journal of Virology*. **2008**. 82(23): 11792-802. **PMID: 18799581.**

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/pubmed/?term=Benmohamed+I

D. Ongoing Research Support:

1. [redacted]
2. R01 AI150091-01. (**BenMohamed, PI**). A Novel Prime/Pull Therapeutic Vaccine Strategy To Prevent Recurrent Genital Herpes. NIH/NIAID Period: **09/01/19 - 08/31/2023.**
3. [redacted]
4. R01 EY026103-01A1. (**BenMohamed, PI**). Mechanisms of CD8+ T Cell Dynamics in Recurrent Ocular Herpetic Disease. NIH/NEI Period: **04/01/16 - 03/31/2020.**
5. R21 AI143326-02. (**BenMohamed, PI**). Impact of Immune Checkpoints Blockade on HSV-1 Neuro-Pathogenesis. NIH/NEI Period: **01/14/19 - 12/31/2021.**
6. R21 AI147499-01 (**BenMohamed, PI**). Protective Immunity Against Recurrent Ocular Herpes Induced with Self-Assembling Protein Nanoparticles. NIH/NIAID. Period: **04/01/19 - 05/31/2021.**

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.

Follow this format for each person. DO NOT EXCEED FOUR PAGES.

NAME	**POSITION TITLE**
Michael J. Buchmeier	**Professor**
eRA COMMONS USERNAME	
mjbuchmeier	

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include

INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Washington State Univ. Pullman, WA	**B.S., M.S.**	**1970, 1972**	**Bacteriology and Public Health**
McMaster Univ., Hamilton, Ontario, Canada	**Ph.D.**	**1976**	**Virology, Immunology**
Scripps Clinic and Research Foundation	**Postdoc**	**1976-1978**	**Viral Immunology and Pathogenesis**

A. Personal Statement

I am virologist and immunologist and with a strong career focus on RNA Viruses. I will bring to the project more than 35 years of experience with the Coronaviruses including the [redacted] and most recently SARS CoV. I have coauthored more than 65 papers on the members of the Coronavirus family, and have made a number of seminal observations including the first demonstration of the location of the receptor binding and membrane fusion domains to the N-terminal and C-terminal halves of the S1-2 open reading frame, the first demonstration of the hypervariable domain localized in the N-terminal S1 domain, and the first detailed cryo-EM structures of the MHV, SARS, and FIP viruses. I have brought the SARS model to me following my move from San Diego to UC Irvine, and we have continued our exploration of the details of the replication of SARS-CoV with studies of the viral subversion of membrane synthesis and assembly to direct the synthesis of double membrane vesicles in infected cells. These vesicles serve as sequestered “factories” where viral macromolecular synthesis is able to take place unimpeded by cellular biosynthesis.

We have also gained extensive experience with in vivo models of the viral infection in the CNS and periphery following MHV infections. The CNS model which we established with Mab resistant variants of the virus forms the basis a model of virally induced demyelination that informs investigators about the details of white matter damage and repair resembling features of MS.

My colleagues and I held a contract and ROI support at my former institution, The Scripps Research Institute, during the period after the appearance of SARS CoV, and my group published more than 20 papers on the structural and cell biology of the virus, and that information will be of value in pursuing the detailed examination of COVID-19. These viruses are, after all close relatives, sharing a major branch of the Coronaviridae. Among the resources we have available are molecular clones of the entire genome of SARS CoV in both E. Coli and BAC vectors. This collection, totaling more than 200 constructs will allow direct one to one comparisons of the similar regions of the two viruses, and will help us to expedite the necessary cloning to produce parallel reagents for COVID-19.

We were able to obtain human clinical samples during the SARS epidemic and after, and will initiate efforts to do the same with the new SARS-CoV-2 virus.

B. Positions and Honors

Positions:

1973-1976 Pre-doctoral research, Mentor: Dr. W. E. Rawls
1977-1978 Fellow, Dept. of Immunopathology, Scripps Clinic and Research Foundation, La Jolla, CA, Supervisor: Dr. M. B. A. Oldstone 1978-1979 Research Associate, Dept. of Immunopathology, Scripps Clinic and Research Foundation (SCRF), La Jolla, CA
1979-1982 Assistant Member (Professor), Dept.of Immunopathology, SCRF, La Jolla, CA
1980-1994 Adjunct Professor, Dept. of Pathology, University of California at San Diego (UCSD), La Jolla, CA
1982-1990 Associate Member (with tenure), Dept. of Immunology, TSRI, La Jolla, CA
1990-1999 Associate Member (with tenure); Dept. of Neuropharmacology, TSRI, La Jolla, CA
1995-1999 Associate Professor, Dept. of Neuropharmacology, TSRI Graduate program in Macromolecular and Cellular Structure and Chemistry
1996-2001 Adjunct Professor, Dept. of Neurology, University of California at Irvine (UCI), Irvine, CA
1997-2019 Adjunct Professor, Dept. of Biology, San Diego State University, San Diego, CA

2000-2007 Professor, Dept. of Molecular and Integrative Neurosciences, TSRI, La Jolla, CA
2008-present, Professor, Departments of Molecular Biology and Biochemistry, and Division of Infectious Disease, Dept of Medicine, UCI, Irvine, CA.

Honors:

1979-1984 Established Investigator Award, American Heart Association,1992-1994 ASM Foundation Lecturer, 1995-1996 Chair-Elect, Division T (RNA Viruses), American Society for Microbiology1996-Elected Fellow of the American Association for the Advancement of Science,1996-1997 Chair, Division T (RNA Viruses), American Society for Microbiology,1997-1998 Alternate Councilor (RNA Viruses), American Society for Microbiology, 1999-2000 Burroughs-Wellcome Visiting Professor, University of New Mexico
2000-2001 Divisional Councilor (RNA Viruses), American Society for Microbiology 2005-Elected Fellow of the American Academy of Microbiology

Contributions to Science

http://scholar.google.com/citations?user=0m195E0AAAAJ&hl=en h-index 68, i10 index 160. 13234 citations
co-author on over 70 papers on Arenaviruses, and more than 65 on Coronaviruses including SARS
Current* and past** editorial boards: mBio*, PloS Pathogen**, The Virology Journal*, BMC Microbiology*, J. Virol.*, Virology*, Virol Immunol*., J. Neurovirol.**, J. Immunol.**, PSEBM** and Intervirol.** (Editor in Chief, 1990-1993), Microbiology and Molecular Biology Reviews (MMBR) Editor in Chief, 2015-2020.
Standing Study Sections: 1991-95 EVR, 2001-05 MIDRC Study Section, 2000-06, National MS Society Peer Review Group A, 1998-02 ORAU-NSF Predoctoral Fellowship review panel
2000, co-Chair, Keystone Conference on Genetics, Pathogenesis and Ecology of Emerging Viral Diseases
2002 Member NIAID Blue Ribbon Panel on Bioterrorism, 2004 co-Chair, Keystone Conference on Bioterrorism and Emerging Infectious Diseases, 2005-20 Editor, Microbiology and Molecular Biology Reviews (MMBR) EIC 2015-2020, 2006-2008 co-Chair, ASM Biodefense and Emerging Infectious Diseases Meeting,
2008-2012 Member NIH-RAC, 2008-present, Member, Biosafety Subcommittee of the RAC.

B. Selected Recent Coronavirus Publications: (from over 160 peer-reviewed publications)

1: Neuman BW, Buchmeier MJ. Supramolecular Architecture of the Coronavirus Particle. Adv Virus Res. 2016;96:1-27. doi: 10.1016/bs.aivir.2016.08.005. Epub 2016 Sep 15. Review. PubMed PMID: 27712621.
2: Angelini MM, Akhlaghpour M, Neuman BW, Buchmeier MJ. Severe acute respiratory syndrome coronavirus nonstructural proteins 3, 4, and 6 induce double-membrane vesicles. mBio. 2013 Aug 13;4(4). pii: e00524-13. doi: 10.1128/mBio.00524-13. PubMed PMID: 23943763; PubMed Central PMCID: PMC3747587.
3: Neuman BW, Angelini MM, Buchmeier MJ. Does form meet function in the coronavirus replicative organelle? Trends Microbiol. 2014 Nov;22(11):642-7. doi: 10.1016/j.tim.2014.06.003. Epub 2014 Jul 15. Review. PubMed PMID: 25037114.
4: Neuman BW, Kiss G, Kunding AH, Bhella D, Baksh MF, Connelly S, Droese B, Klaus JP, Makino S, Sawicki SG, Siddell SG, Stamou DG, Wilson IA, Kuhn P, Buchmeier MJ. A structural analysis of M protein in coronavirus assembly and morphology. J Struct Biol. 2011 Apr;174(1):11-22. doi: 10.1016/j.jsb.2010.11.021. Epub 2010 Dec 3. PubMed PMID: 21130884; PubMed Central PMCID: PMC4486061.
5: Serrano P, Johnson MA, Chatterjee A, Neuman BW, Joseph JS, Buchmeier MJ, Kuhn P, Wüthrich K. Nuclear magnetic resonance structure of the nucleic acid-binding domain of severe acute respiratory syndrome coronavirus nonstructural protein 3. J Virol. 2009 Dec;83(24):12998-3008. doi: 10.1128/JVI.01253-09. Epub 2009 Oct 14. PubMed PMID: 19828617; PubMed Central PMCID: PMC2786856.
6: Cornillez-Ty CT, Liao L, Yates JR 3rd, Kuhn P, Buchmeier MJ. Severe acute respiratory syndrome coronavirus nonstructural protein 2 interacts with a host protein complex involved in mitochondrial biogenesis and intracellular signaling. J Virol. 2009 Oct;83(19):10314-8. doi: 10.1128/JVI.00842-09. Epub 2009 Jul 29. PubMed PMID: 19640993; PubMed Central PMCID: PMC2748024.
7: Neuman BW, Adair BD, Yeager M, Buchmeier MJ. Purification and electron cryomicroscopy of coronavirus particles. Methods Mol Biol. 2008;454:129-36. doi: 10.1007/978-1-59745-181-9_12. PubMed PMID: 19057879.
8: Chatterjee A, Johnson MA, Serrano P, Pedrini B, Joseph JS, Neuman BW, Saikatendu K, Buchmeier MJ, Kuhn P, Wüthrich K. Nuclear magnetic resonance structure shows that the severe acute respiratory syndrome coronavirus-unique domain contains a macrodomain fold. J Virol. 2009 Feb;83(4):1823-36. doi: 10.1128/JVI.01781-08. Epub 2008 Dec 3. PubMed PMID: 19052085; PubMed Central PMCID: PMC2643772.
9: Neuman BW, Joseph JS, Saikatendu KS, Serrano P, Chatterjee A, Johnson MA, Liao L, Klaus JP, Yates JR 3rd, Wüthrich K, Stevens RC, Buchmeier MJ, Kuhn P. Proteomics analysis unravels the functional repertoire of coronavirus nonstructural protein 3. J Virol. 2008 Jun;82(11):5279-94. doi: 10.1128/JVI.02631-07. Epub 2008 Mar 26. PubMed PMID: 18367524; PubMed Central PMCID: PMC2395186.
10: Serrano P, Johnson MA, Almeida MS, Horst R, Herrmann T, Joseph JS, Neuman BW, Subramanian V, Saikatendu KS, Buchmeier MJ, Stevens RC, Kuhn P, Wüthrich K. Nuclear magnetic resonance structure of the N-terminal domain of

nonstructural protein 3 from the severe acute respiratory syndrome coronavirus. J Virol. 2007 Nov;81(21):12049-60. Epub 2007 Aug 29. PubMed PMID: 17728234; PubMed Central PMCID: PMC2168779.
11: Burrer R, Neuman BW, Ting JP, Stein DA, Moulton HM, Iversen PL, Kuhn P, Buchmeier MJ. Antiviral effects of antisense morpholino oligomers in murine coronavirus infection models. J Virol. 2007 Jun;81(11):5637-48. Epub 2007 Mar 7. PubMed PMID: 17344287; PubMed Central PMCID: PMC1900280.
12: Neuman BW, Stein DA, Kroeker AD, Moulton HM, Bestwick RK, Iversen PL, Buchmeier MJ. Inhibition and escape of SARS-CoV treated with antisense morpholino oligomers. Adv Exp Med Biol. 2006;581:567-71. Review. PubMed PMID: 17037599.
13: Burrer R, von Herrath MG, Wolfe T, Rempel JD, Iglesias A, Buchmeier MJ. Autoantibodies exacerbate the severity of MHV-induced encephalitis. Adv Exp Med Biol. 2006;581:399-402. Review. PubMed PMID: 17037567.
14: Neuman BW, Adair BD, Yoshioka C, Quispe JD, Milligan RA, Yeager M, Buchmeier MJ. Ultrastructure of SARS-CoV, FIPV, and MHV revealed by electron cryomicroscopy. Adv Exp Med Biol. 2006;581:181-5. PubMed PMID: 17037527.
15: Neuman BW, Adair BD, Yoshioka C, Quispe JD, Orca G, Kuhn P, Milligan RA, Yeager M, Buchmeier MJ. Supramolecular architecture of severe acute respiratory syndrome coronavirus revealed by electron cryomicroscopy. J Virol. 2006 Aug;80(16):7918-28. PubMed PMID: 16873249; PubMed Central PMCID: PMC1563832.

D. Research Support

Ongoing Research Support: Discretionary Budget: Current Balance $166,633 as of 20 Feb, 2020
for discovery targeting RNA viruses.

Completed Research Support

1 U54 AI065359-04 Barbour, A. (Assoc. Director/Project Leader) 5/20/06 – 4/30/14 NIH/NIAID
Pacific-Southwest Center for Biodefense & Emerging Infectious Diseases
This program-project group brings together investigators with expertise in arenavirus molecular biology and pathogenesis, and receptor biology to address novel questions pertinent to development of new approaches to arenavirus vaccines and antivirals.

1 RO1 AI059799-04 Buchmeier (PI) 7/1/05 - 3/31/10
NIH/NIAID
Human T-cell Epitopes in SARS
The major goal of this project is to identify the human MHC restricted Class I and Class II epitopes derived from the complete proteome of the SARS CoV. Also, to construct vaccinia expression vectors representing the entire 3 prime end of the genome downstream of ORF 1a/1b for the purpose of testing the [redacted] to understand the anti-SARS immune response and designing anti-SARS immune based antiviral therapy.

HHSN266200400023C Sette (Co-Investigator) 3/31/04 - 9/30/09
NIH Contract
Large Scale Antibody and T Cell Epitope Discovery Program
The major goal of this project is the discovery and validation of cytotoxic and helper T cell epitopes presented by HLA class I and class II MHC molecules, respectively, that are derived from a group of prevalent arenaviruses with known potential for causing disease in humans, and representative of a diverse set of arenavirus phylogenetic groups.

NIH Contract No. HHSN266200400058C Kuhn (Co-PI) 6/29/04 - 6/28/09
Functional and structural proteomics of the SARS-CoV
This project aims for the complete functional and structural characterization of all proteins related to SARS-CoV using a comprehensive, systems approach using extensive functional and structural proteomics experience of the participating investigators.

OMB No. 0925-0001 and 0925-0002 (Rev. 03/2020 Approved Through 02/28/2023)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Donald Forthal

eRA COMMONS USER NAME (credential, e.g., agency login): DONALDFORTHAL

POSITION TITLE: Professor of Medicine and Molecular Biology & Biochemistry

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of California, Los Angeles	AB	1971	Linguistics
University of California, Irvine School of Medicine	MD	1979	Medicine
University of California, San Francisco, CA	Internship	1980	Pediatrics
UCLA/Harbor Medical Center, Torrance, CA	Residency	1982	Pediatrics
LAC/USC Medical Center, Los Angeles, CA	Fellowship	1984	Infectious Diseases

A. Personal Statement

Dr. Forthal will help Dr. BenMohamed with COVID-19 patients recruitment and identification of symptomatic and asymptomatic patients as described in Aim 1 of this Pan-Coronavirus vaccine R01 proposal. Dr. Forthal and Dr. BenMohamed laboratories are located in same building which facilitates daily interaction.

Dr. Forthal has been involved with research in the field of viral immunology for over two decades, beginning with his time as an Epidemic Intelligence Service Officer with the Centers for Disease Control and continuing to his present directorship of a laboratory focused on antibody responses to viruses, particulary HIV and related lentiviruses.

Dr. Forthal and his laboratory have been at the forefront of investigating Fc-Fc receptor interactions in the setting of lentivirus and other viral infections. The work contributed by the Forthal laboratory has, in many ways, offered a new view of antibody function and has opened the door to much research on the role of Fc-Fc receptor interactions in preventing or modulating infections. Recently, Dr. Forthal has extended his studies to include flaviviruses.

Over the last several years, Dr. Forthal has received continuous funding support from NIH and various other institutions. He has served as a mentor for numerous research and clinical trainees.

Dr. Forthal is also a clinician who cares for patients with HIV and other infections.

B. Positions

1984-1987: Epidemic Intelligence Service Officer (Viral Special Pathogens), Centers for Disease Control
1987: AIDS Coordinator, African Region, World Health Organization, Brazzaville, Congo
1987-1989: Infectious Diseases practice
1989-1994: Assistant Clinical Professor, University of California, Irvine School of Medicine
1994-2001: Assistant Professor of Medicine, University of California, Irvine School of Medicine
2001-2012: Associate Professor of Medicine, University of California, Irvine School of Medicine
2002-present: Chief, Division of Infectious Diseases, University of California, Irvine School of Medicine
2004-present: Faculty, Center for Virus Research, University of California, Irvine
2005-present: Faculty, Institute for Immunology, University of California, Irvine
2012-present: Professor of Medicine, University of California, Irvine School of Medicine
2014-present: Professor of Molecular Biology & Biochemistry, University of California, Irvine School

of Biological Sciences

Honors

2008-present: Ad hoc member, many special emphasis panels (NIH)
2009-2013: Standing member, VACC study section (NIH)
2015-2018: Standing member, AIP study section (NIH)
2013-2018**:** Member, AIDS Vaccine Research Subcommittee (advisory panel to NIH)
2014-present: Editorial Board, Journal of Immunology
2018-present: Associate editor, Open Forum Infectious Diseases

C. Contribution to Science

Antibodies have multiple functions in the setting of viral infections. The Forthal laboratory has been interested in non-neutralizing antibodies and the role they play in preventing lentiviral infections. This led to a focus on Fc-Fc receptor (FcR) interactions and the anti-viral effects that such interactions engender. Of particular impact has been our development of the antibody-dependent cell-mediated virus inhibition (ADCVI) assay. This assay has provided a means of measuring the net effect of FcR-mediated antibody functions affecting viruses, such as measles virus and HIV-1, in a manner that is biologically relevant. Among several publications, four are highlighted below:

1. **Forthal** DN, Landucci G, Daar ES. Antibody from patients with acute HIV infection inhibits primary strains of HIV-1 in the presence of natural killer or macrophage effector cells. *J Virol* 2001;75:6953-61. PMID: 11435575. PMCID: PMC114423

2. Hessell AJ, Hangartner L, Hunter M, Havenith CEG, Beurskens FJ, Bakker JM, Lanigan C, Landucci G, **Forthal** DN, Parren PWHI, Marx PA, Burton DR. Fc receptor but not complement binding is important in antibody protection against HIV. *Nature* 2007; 449:101-104. PMID: 17805298.

3. Vaccari M, Fourati S, Gordon S, Brown D, Bissa M, Schifanella L, Silva de Castro I, Doster M, Galli V, Omsland M, Fujikawa D, Gorini G, Liyanage N, Trinh H, McKinnon K, Foulds K, Keele B, Roederer M, Koup R, Shen X, Tomaras G, Wong MP, Munoz K, Gach J, **Forthal DN**, Montefiori DC, Venzon D, Felber B, Rosati M, Pavlakis G, Rao M, Sekaly R-P, Franchini G. HIV vaccine candidate activation of hypoxia and inflammasome in CD14+ monocytes is associated with a decreased risk of SIVmac251 acquisition. *Nature Med* 2018; 24:847-56. PMID: 29785023. PMCID: PMC5992093

4. **Forthal DN**, Finzi A. Blocking HIV-1 replication: are Fc-Fcγ receptor interactions required? (Invited commentary). ***J Clin Invest*** 2019; 129:53-4. PMID: 30475231. PMCID: PMC6307933.

[redacted]

1. **Forthal DN**, Gabriel EE, Wang A, Landucci G, Phan TB. FcγRIIIa genotype and behavioral risk interact to predict HIV infection rate following recombinant gp120 vaccination. *Blood* 2012;120:2836-42. PMID: 22915639. PMCID: PMC3466964

2. Gorlani A, **Forthal DN**. Antibody-dependent enhancement and the risk of HIV infection. *Current HIV Res 2013*;11:421-6 (Invited review). PMID: 24191936.

3. Sholukh AM, Siddappa NB, Shanmuganathan V, Hemashettar G, Lakhashe SK, Rasmussen RA, Watkins JD, Vyas HK, Thorat S, Brandstoetter T, Mukhtar MM, Yoon JK, Novembre FJ, Villinger F, Landucci G, **Forthal DN**, Ratcliffe R, Tuero I, Robert-Guroff M, Polonis VR, Bilska M, Montefiori DC, Johnson WE, Ertl HC, Ruprecht RM. Passive immunization of macaques with polyclonal anti-SHIV IgG against a heterologous tier 2 SHIV: outcome depends on IgG dose. *Retrovirology* 2014;11:8. PMID: 24444350. PMCID: PMC3905655

4. Gach JS, Venzon D, Vaccari M, Keele BF, Franchini G, **Forthal DN**. The relationship between vaccine-induced antibody capture of infectious virus and infection outcomes following low-dose, repeated rectal challenge with SIVmac251. *J Virol* 2016;90:8487-95. PMID: 27440881. PMCID: PMC5021405

Several other aspects of HIV immunity centered on antibody functions in general and on Fc-FcR interactions in particular, including Fc-FcRN interactions, have been investigated by the Forthal laboratory. These include potentially critical issues related to pathogenesis and protection and a recent publication that serves as the basis for the proposed research:

1. Gupta S, Gach JS, Becerra JC, Phan TB, Pudney J, Moldoveanu Z, Joseph SB, Landucci G, Supnet MJ, Ping L-H; Corti D, Moldt D, Hel Z, Lanzavecchia A, Ruprecht RM, Burton DR, Mestecky J, Anderson DJ and **Forthal DN**. The neonatal Fc receptor (FcRn) enhances human immunodeficiency virus type 1 (HIV-1) transcytosis across epithelial cells. *PLoS Pathogens* 2013; 9:e1003776. PMID: 24278022. PMCID: PMC3836734

[redacted]

3. Gach JS, Bouzin M, Wong MP,Gorlani A, Yu K-T, Sharma B, Gratton E, **Forthal DN**. Human immunodeficiency virus type-1 (HIV-1) evades antibody-dependent phagocytosis. *PLoS Pathogens* 2017;13:e1006793. PMID: 29281723. PMCID: PMC5760106

4. Gach JS, Mara KJV, LaBranche CC, van Gils MJ, McCoy LE, Klasse PJ, Montefiori DC, SandersRW, Moore JP, and **Forthal DN**. Antibody responses elicited by immunization with BG505 trimer-immune complexes. *J Virol* 2019;129:53-4. PMID: 30475231. PMCID: PMC6798112

Other relevant publications:

[redacted]

Published work can be found at: http://www.ncbi.nlm.nih.gov/pubmed/?term=Forthal

D. Research Support

Ongoing Research Support

R01 AI118581 Forthal (PI) 06/15/2015-06/14/2020
"The role of antibody and the Fc neonatal receptor in transmitted/founder strain selection"
The goal is to determine if FcRn engagement by SIV-IgG immune complexes results in founding strain selection and contributes to enhanced infection.

R21 AI149255 Forthal (PI) 01/23/2019-12/31/2021

[redacted]

Recently Completed Research Support

R01 AI102715 Forthal (PI) (NCE)
NIH Allergy and Infectious Diseases 7/6/2012-6/30/2016

[redacted]

R21 AI079775 Peterson, Forthal (co-PIs) 05/01/2009-04/30/2015 (NCE)
NIH Allergy and Infectious Diseases
"Iron Starvation: A novel strategy for HIV and Chlamydia microbicides"
Goal is to measure anti-HIV and anti-Chlamydial activity of iron-binding compounds for use as topical microbicides.

U54 AI65359 Barbour (PI) 05/2007-04/2015 (NCE)
NIH Allergy and Infectious Diseases
Pacific Southwest Center for Biodefense and Emerging Infections
Administer and finance projects at a consortium of 16 universities and research institutes in California, Arizona, Nevada and Hawaii. Its mission will be to bolster basic biomedical research into bioterrorism agents, such as those that cause anthrax and botulism, and naturally occurring infectious diseases.
Role: Associate Director

R01 AI038518-16A2 Overbaugh (PI)
NIH through Fred Hutchinson Cancer Research Center 3/1/2010 – 2/28/2015
"Early and Reinfection in High Risk Women"
Goal is to explore the relationships between anti-viral antibody activity and primary or re-infection in women at risk of acquiring HIV.
Role: PI at UCI

R01 AI090656 Forthal (PI) 06/14/2010-05/31/2014
"Broadly Reactive Antibodies against Chimeric Virus-Host Antigens"
Goal is to identify antibodies that react with epitopes that are chimeric between host and HIV envelope.

OMB No. 0925-0001 and 0925-0002 (Rev. 03/2020 Approved Through 02-28-2023)

BIOGRAPHICAL SKETCH

NAME: Sebastian Dominik Schubl, MD, FACS

POSITION TITLE: HS Associate Clinical Professor of Surgery

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Johns Hopkins University	B.A.	05/1999	Molecular Biology
University of Virginia, School of Medicine	M.D.	05/2004	Doctor of Medicine
MCL/Louisiana State University		08/1998	Internship in Surgery
NYP/Weill Cornell Medical College Memorial Sloan Kettering Cancer Center		6/2011	Residency in Surgery
University of California, Irvine		7/2016	Fellowship in Surgical Critical Care

A. Personal Statement

I will help Dr. BenMohamed with COVID-19 patients recruitment and identification of symptomatic and asymptomatic patients as described in Aim 1 of this Pan-Coronavirus vaccine R01 proposal.

I have the expertise, leadership, training, and motivation necessary to successfully carry out the proposed research project. I have authored over 65 peer-reviewed publications as well as several book chapters and have presented at a variety of national meetings on a diverse range of research topics. I serve on several research-oriented committees in national and international societies including the Scientific Studies Committee for the Surgical Infection Society and as Chair of the Publications Committee for the Chest Wall Injury Society. I have written and presented several projects including basic science work during my time as a research fellow at Weill Cornell College of Medicine as well as outcomes research, meta-analyses, systematic reviews, multi-center trials and large database studies. I serve in an administrative capacity within hospital leadership which provides insight and access to resources. I have collaborated with a wide range of researchers from multiple backgrounds executing projects. I excel at the administrative and project planning phase of the work, as I have found that the “good idea” is often the easy part but it is in the execution of that idea that the true work lies. I am particularly proud that nearly every paper that I have written is first authored by a resident or medical student as I take my role as a mentor very seriously and find enormous satisfaction in the training of the next generation of physician scientists.

1. Grigorian A, Schubl SD, Barrios C, Joe V, Dolich M, Lekawa M, Nahmias J. Association of Heparin-Induced Thrombocytopenia With Bacterial Infection in Trauma Patients. JAMA Surg. doi:10.1001/jamasurg.2018.1652
2. Delaplain P, Barrios C, Spencer D, Lekawa M, Schubl SD, Dosch A, Grigorian A, Pejcinovska M, Nahmias J. The use of computed tomography imaging for abdominal seatbelt sign: a single-center, prospective evaluation. Injury. DOI: https://doi.org/10.1016/j.injury.2019.10.089
3. Delaplain PT, Philips JL, Barie PS and Schubl SD. No reduction in surgical site infection from postoperative antibiotics in facial fractures, regardless of duration or anatomic location: a systematic review and meta-analysis. Surgical Infections. 2019 Sept 17

B. Positions and Honors

Hospital and Academic Employment

2011-2016 Clinical Faculty Instructor, Department of Surgery; Weill Cornell Medical College
2011-2016 Clinical Faculty Instructor, Surgery and Medicine; Ross University School of Medicine
2011-2016 Attending Surgeon, Jamaica Hospital, Department of Surgery
2012-2016 Trauma Medical Director, Jamaica Hospital Trauma Center
2017-2019 HS Assistant Clinical Professor, Department of Surgery; University of California Irvine
2017- Chief, Division of Emergency General Surgery, Department of Surgery
2018- Bed Czar, UCI Health Executive Leadership
2018- Clerkship Director, Surgery Electives; University of California Irvine SOM
2019- HS Associate Clinical Professor, Department of Surgery; University of California Irvine
2019- Medical Director of Surgical Telemetry & Surgical Step-Down Units
2020- Medical Director, Patient Progression

Other Experience and Professional Memberships

2010- SIS, Surgical Infection Society, Member
2011- EAST, Eastern Association for the Surgery of Trauma, Member
2011- ACS, American College of Surgeons; 3216672; Fellow
2016- SCCM, Society for Critical Care Medicine, 291181, Member
2016- AAST, American Association for the Surgery of Trauma, Fellow
2017- CWIS, Chest Wall Injury Society, 580, Member
2017- SCCACS, Southern California Chapter of the American College of Surgeons; Member
2017- Member, Items Committee, Society for Critical Care Medicine
2017- Member, Scientific Studies Committee, Surgical Infection Society
2018- Chair, Publications Committee, Chest Wall Injury Society
2018- Member, Executive Council, Chest Wall Injury Society
2019- Member, Manuscript and Literature Review Committee, EAST

2016- Member, Trauma Performance Improvement Committee, UC Irvine Health
2016- Member, Education Committee for the Department of Surgery, UC Irvine School of Medicine
2016- Member, Utilization Management Committee, UC Irvine Health
2016- Member, Surgical Critical Care Competency Committee, UC Irvine Health
2016- Member, Antibiotic Stewardship Committee, UC Irvine Health
2017- Member, Program Evaluation Committee for General Surgery Residency, UC Irvine Health
2017- Member, Anesthesia Critical Care Competency Committee, UC Irvine Health
2018- Member, Committee of Clerkship Directors, UC Irvine School of Medicine
2019- Member, OR Governance Committee, UC Irvine Health
2019- Member, Value Analysis Committee, UC Irvine Health
2020- Member, Chief Operating Officer Search Committee, UC Irvine Health
2020- Member, Chief Financial Officer Search Committee, UC Irvine Health

Honors

2008 Association of Academic Surgeons/Society of University Surgeons Resident Research Award
2018 ARIISE Award Nominee - Accountability
2018 EAST Mentorship Program with Joseph Farhat MD, FACS, North Memorial Medical Center
2019 ARIISE Award Nominee - Service
2019 UC Irvine School of Medicine Humanitarian in Medicine Faculty Award

C. Contribution to Science

1. My early publications were funded by a highway safety grant from the state of New York and revolved around the risk factors, injury patterns and management of pedestrians involved in vehicular trauma. These early studies taught me much about the rigors of data collection and the proper execution of a prospectively maintained registry and the critical skills necessary for proper collaboration with a team of researchers. Beyond the research we were able to do, we were also responsible for building the largest

pedestrian trauma database available that cataloged the behaviors and circumstances of the trauma from the perspective of the pedestrian, a data set that is still being added to and serves a myriad of researchers interested in this topic in New York City.

a. Melissa K. James, PhD, Shi-Wen Lee, DO, Jennifer A. Minneman, MD, Maureen D. Moore MD, Taylor R. Klein, BS, R. Jonathan Robitsek, PhD, Phillip S. Barie, MD, MBA , Sebastian D. Schubl, MD. “Variability in CT imaging of blunt trauma among ED physicians, surgical residents, and trauma surgeons.” Journal of Surgical Research. February 2017.
b. Melissa K James PhD, Sebastian Schubl MD, Michael P. Francois BS, Geoffrey K. Doughlin MD, FACS, Shi-Wen Lee DO. “Introduction of Pan-scan protocol for blunt trauma activations: what are the consequences?” American Journal of Emergency Medicine. 2016 Sept 22. pii: S0735-6757(16)30605-2. DOI: 10.1016/j.ajem.2016.09.027.
c. S.D. Schubl, T.R. Klein, R.J. Robitsek, S. Trepeta, K. Fretwell, D. Seidman, M. Gottlieb. “Temporal Bone Fracture: Evaluation in the Era of Modern Computed Tomography”. Injury. 2016 Sept; 47(9):1893-7 PMID: 27387791. DOI: 10.1016/j.injury.2016.06.026

2. As I transitioned to UC Irvine I engaged with a team of of collaborators to undertake significant work in outcomes research using a variety of large databased both at the institutional level and the national one. Working largely with residents in the Department of Surgery we were able to address a variety of unanswered questions in the worlds of surgical critical care, trauma and emergency general surgery. Employing sophisticated analytics and statistical methodologies we were able to analyze large data sets and produced a large volume of peer-reviewed publications.
    a. Abate M, Grigorian A, Nahmias J, Schubl S, Kuncir E, Lekawa M. Differing Risk of Mortality in Trauma Patients with Stab Wounds to the Torso: Treating Hospital Matters. JAMA Surgery. Accepted.
    b. Delaplain P, Barrios C, Spencer D, Lekawa M, Schubl S, Dosch A, Grigorian A, Pejcinovska M, Nahmias J. The use of computed tomography imaging for abdominal seatbelt sign: a single-center, prospective evaluation. Injury. DOI: https://doi.org/10.1016/j.injury.2019.10.089
    c. Grigorian A, Schubl S, Scolaro J, Jasperse N, Gabriel V, Hu A, Petrosian G, Joe V, Nahmias J. No increased risk of acute osteomyelitis associated with closed or open long bone shaft fracture. Journal of Clinical Orthopedics and Trauma. Vol 10. Oct 2019 S133-138.

3. Finally, due to my long involvement with the Surgical Infection Society, mostly though my mentor, Dr, Philip S, Barie, who was my instructor during residency, I have a keen interest in the study of infectious diseases from the perspective of a surgeon. This work is still very much ongoing as I am a member of the scientific studies committee of the SIS. This work has been collaborative across multiple institutions and has been under the guidance of a mentor that has a long and very well-respected bibliography that spans several decades.
    a. Schubl SD, Raymond L, Robitsek RJ, Bagheri F. (2016) Isolated Clostridium difficile Small Bowel Enteritis in the Absence of Predisposing Risk Factors, Surgical Infections Case Reports 1.1, 1-3, DOI:10.1089/crsi.2016.0006.
    b. Amit Basu MD, Taylor Klein BS, R. Jonathan Robitsek PhD, Jeffrey Chan MD, Alfredo Wong MD, David Sammett MD, PhD, Katherine McKenzie DO, K. Geoffrey Doughlin MD, Kenneth Fretwell MD, and Sebastian D. Schubl MD. “Effect of the Affordable Care Act on Financial Margins and Access to Care for Appendectomy and Cholecystectomy”. Journal American College of Surgeons, 223(4):e34; Oct 2016.
    c. Grigorian A, Schubl S, Barrios C, Joe V, Dolich M, Lekawa M, Nahmias J. Association of Heparin-Induced Thrombocytopenia With Bacterial Infection in Trauma Patients. JAMA Surg. doi:10.1001/jamasurg.2018.1652
    d. Gabriel V, Grigorian A, Nahmias J, Won E, Bernal N, Barrios C, Schubl S. Risk Factors for Postoperative Sepsis and Septic Shock in Patients Undergoing Emergency Surgery. Surgical Infections. Accepted.
    e. Delaplain PT, Philips JL, Barie PS and Schubl SD. No reduction in surgical site infection from postoperative antibiotics in facial fractures, regardless of duration or anatomic location: a systematic review and meta-analysis. Surgical Infections. 2019 Sept 17

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

CRAFT-COVID Grant Schubl (Co-PI) 05/01/2020-07/01/2021
Serologic Surveillance of Health Care Workers for SARS-CoV-2 Antibodies During COVID-19 Pandemic Using a Coronavirus Antigen Microarray. Dean's level funding for validation of a protein micro-array to detect antibody reactivity in a health care worker population.

UCOP R00RG2646 Schubl (Co-PI) 05/01/2020-07/01/2021
COVID-19 Research Seed Funding Grant. Serosurveillance of Health Care Workers for COVID-19 Using a Coronavirus Antigen Microarray. UC Office of President emergency seed funding for COVID-a9 related research.

UROP 75192S1 Schubl (PI) 07/01/2018-06/30/2019
The utility of Near Infrared Spectroscopy to detect Necrotizing Soft Tissue Infections
The goal of this study is to determine the utility and sensitivity of a hand-held oxygen tissue tension monitor based of infrared spectroscopy to differentiate necrotizing soft tissue infections from simple cellulitis
Role: PI

UROP 75192S1 Schubl (PI) 07/01/2019-06/30/2020
Renewal of the above grant for ongoing study.

Completed Research Support

T32RR021312-06 KC Kent (PI) 07/01/2010-06/30/2015
Understanding the role of protein kinase C delta in the developed of aortic aneurysms.
Successful renewal of existing T32 NIH grant for the Kent lab at Weill Cornell Medical College to continue studying aneurysm formation in both a rat and a moue model for vascular aneurysms including the role of protein kinase C delta in the inflammatory cascade central to arterial wall remodeling and deformation.
Role: Research fellow

HS1-2015-Jamaica Hosp-00182-(041) Schubl (PI) 01/01/2013-12/31/2013
New York State Governors Traffic Safety Committee Highway Safety Grant to study pedestrian trauma. Studied patterns of behavior and risk factors from both the pedestrian as well as the driver's perspective to better understand the circumstances of pedestrian trauma in the borough of Queens, NYC.
Role: PI

HS1-2015-Jamaica Hosp-00182-(041) Schubl (PI) 01/01/2014-12/31/2014
Renewal of the above grant for ongoing study.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Anthony Bart Nesburn

eRA COMMONS USER NAME (credential, e.g., agency login): anesburn

POSITION TITLE: : Adjunct Professor/Vice Chair of Research

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of California at Los Angeles (UCLA)(Magna Cum Laude)	BA	1986	Premed Science
Harvard medical School, Boston (Cum Laude)	MD	1960	Medicine
Boston City Hospital (Harvard Service)	DEA	1960-61	Internship
Boston Children's Hospital with John Enders, PhD		1965-66	Fellowship Infectious Diseases
Massachusetts Eye & Ear Infirmary, Boston		1966-68	Resident Ophthalmology

A. Personal Statement

I am a clinician-scientist at the Gavin Herbert Institute, University of California Irvine, where I serve as Vice Chair for Research. I have been collaboration with Dr. BenMohamed for over 20 years.

I have special expertise in viral infections in humans (both high-level patient consultation and clinical trials). In my 30 years of R01 grant support I utilized [redacted] of humans. For four years, I served as a Data and Safety Monitor to the HEDS study—a large multi-institutional human clinical trial.

I have made several contributions to science (CtS) throughout my career that have remained relevant decades later. I was intimately involved in the discovery of the first antiviral drug, idox-uridine and showing its efficacy against experimental ocular herpes virus infection [redacted] For many years it was the only antiviral approved for human use (CtS #1 below). I discovered that [redacted] used for many years to study primary ocular herpes simplex infection actually exhibits chronic recurrences of HSV keratitis and shedding just like humans. This model remains the primary test model for HSV recurrence (CtS #2 below). I was the first to show that HSV was latent in the [redacted] between reactivation episodes (CtS #3 below).

In 1998 I hired and started collaborating with a young, innovative immunologist and vaccinologist trained at the Institute Pasteur, Lbachir BenMohamed. I have supplied the human medical insight and knowledge of animals models of ocular HSV in Dr. BenMohamed's systematic investigation to understand the crucial factors of the viral immune responses and harness those that are protective to find a safe and effective vaccination strategy against recurrence HSV [redacted] and humans (CtS #5 below). I have been an advisor to Dr. BenMohamed in regard to [redacted] of infectious disease and in regard to FDA clinical trials for HSV and Coronavirus.

B. Positions and Honors

PROFESSIONAL EXPERIENCE

1961 Research Fellow in Ophthalmology, Harvard Medical School, Boston.

1964-1966	Research Fellow, Harvard University, Research Division of Infectious Disease, Dr. John F. Enders, Children's Medical Center, Boston. Instructor, Harvard Medical School.
1966-1968	Head, Virology Laboratory, Howe Laboratory of Ophthalmology, Massachusetts Eye & Ear Infirmary.
1968-1984	Assistant, Associate and Clinical Professor of Ophthalmology, USC Medical School.
1968-1984	Director, Virology Lab, Doheny Eye Foundation/USC School of Medicine.
1972 & 1976	Member, 1st, 2nd, National Eye Institute (NEI) Program Planning Corneal Task Force.
1973-1976	Member, Vision Research Program Committee, National Eye Institute.
1980-1983	Chairman (3rd) NEI, Corneal Task Force, Program Planning Subcommittee.
1984-1985	Clinical Professor of Ophthalmology, USC School of Medicine, Los Angeles.
1985-2002	Clinical Professor of Ophthalmology, UCLA School of Medicine, Los Angeles.
1985-2002	Director of Ophthalmology Research Laboratories-Cedars-Sinai Medical Center, Los Angeles.
1988	Committee Chairman, "New Research Strategies for Corneal Diseases Research, "NEI, Reporting to the NAEC for Program Planning 1990-1992, Washington, D.C.
1988-1993	Data & Safety Monitoring Committee – NIH Herpes Eye Disease Study (HEDS-1)
1997-2000	Member, National Advisory Eye Council, National Institutes of Health, Washington, D.C.
2002-Pres.	Adjunct Professor and Vice Chair for Research, Gavin Herbert Eye Institute, UC Irvine

C. Contributions to Science

1. Involved in the discovery of the first antiviral drug to work in-vivo, idox-uridine.

Dr. Nesburn was intimately involved in the discovery of the first antiviral drug, idox-uridine and showing its efficacy against experimental ocular herpes virus infection [redacted] It was the first FDA-approved antiviral medication and for many years it was the only antiviral approved for human use.

In 1960 there were no antiviral drugs that worked *in vivo*. As a pre-residency fellow at the Massachusetts Eye and Ear Infirmary I asked Dr. Herbert Kaufman if I could do an experiment in [redacted] model of acute ocular HSV to test the effect of dropping dilute iodine drops every 2 hours around the clock. Iodine scrub of the HSV infected cornea was a common clinical treatment in humans. Dr. Kaufman added another treatment group to the iodine and control groups using a substance just reported in *Proc Soc* as having promising in vitro antiviral properties iodo-deoxy uridine (IDU). [redacted] clear after 48 hours of treatment while the iodine and saline treated groups had severe HSV keratitis. This finding helped to spawn development of other topical antiherpes drugs, trifluridine and oral anti-virals such as acyclovir. **The follow-on drugs to IDU are still used clinically to treat primary and recurrent HSV keratitis worldwide.**

Kaufman HE, **Nesburn AB**, Maloney ED. IDU therapy of herpes simplex. *Arch Ophthalmol*. 1962 May;67:583-91. PMID:14454444

Nesburn AB, Robinson C, Dickinson R. Adenine arabinoside effect on experimental idoxuridine-resistant herpes simplex infection. *Invest Ophthalmol*. 1974 Apr;13(4):302-4. PMID:4362055

Nesburn AB, Willey DE, Trousdale MD. Effect of intensive acyclovir therapy during artificial reactivation of latent herpes simplex virus. *Proc Soc Exp Biol Med*. 1983 Mar;172(3):316-23. PMID:6302707

[redacted]

[redacted]

[redacted]

4. With Drs. D Rock and S. Wechsler we were was the first to show at a meeting and second to publish that LAT was the only actively transcribed RNA during HSV latency.

The LAT transcript was difficult to find at first until we used in-situ hybridization to show the RNA signal in latently

[redacted]

Perng GC, Jones C, Ciacci-Zanella J, Stone M, Henderson G, Yukht A, Slanina SM, Hofman FM, Ghiasi H, **Nesburn** AB, Wechsler SL. Virus-induced neuronal apoptosis blocked by the herpes simplex virus latency-associated transcript. *Science*. 2000 Feb 25;287(5457):1500-3. PMID:10688801

5. With RO1 grants from NEI began to developing a vaccine against HSV primary and recurrent infection.

In 1990 Dr. Nesburn's NEI-supported research involved using locally administered HSV glycoprotein D and then in 1994 glycoproteins B and D as a therapeutic vaccine to significantly reduce HSV ocular shedding in latently [redacted] In 2001 Dr. Nesburn started collaborating with a young, innovative immunologist and vaccinologist trained at the Institute Pasteur, Lbachir BenMohamed. Dr. Nesburn has supplied the human medical insight and knowledge of [redacted] of ocular HSV in Dr. BenMohamed's quest to understand the crucial factors of the ocular HSV immune responses and harness those that are protective to find a safe and effective vaccination strategy against recurrence ocular HSV in [redacted] and humans.

Nesburn AB, Ghiasi H, Wechsler SL. Ocular safety and efficacy of an HSV-1 gD vaccine during primary and latent infection. *Invest Ophthalmol Vis Sci.* 1990 Aug;31(8):1497-502. PMID:2167298

[redacted]

25617474.

Arif Azam Khan; Ruchi Srivastava; Doran Spencer; Daniel Fremgen; Hawa Vahed; Patricia P. Lopes; Thanh T Pham; Charlie Hewett; Jasmine Kuang; Nicolas Ong; Lei Huang; Vanessa M. Scarfone, **Anthony B. Nesburn**; Steven L. Wechsler & BenMohamed L**.** Phenotypic and Functional Characterization of Herpes Simplex Virus Glycoprotein B Epitope-specific Effector and Memory CD8+ T Cells from Ocular Herpes Symptomatic and Asymptomatic Individuals. *The Journal of Virology*. **2015**. 89(7): 3776-92. PMID: 25609800.

Complete List of Published Work in My Bibliography: http://www.ncbi.nlm.nih.gov/pubmed/?term=Nesburn

D. Additional Information: Research Support and/or Scholastic Performance

None.

BIOGRAPHICAL SKETCH

NAME: McLaren, Christine E.

eRA COMMONS USER NAME (credential, e.g., agency login): cmclaren

POSITION TITLE: Professor of Biostatistics

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
California State University, San Jose, CA	BS (Honors)	06/69	Mathematics
Stanford University, Palo Alto, CA	MA	06/70	Mathematics Education
Case Western Reserve University, Cleveland, OH	MS	06/76	Mathematical Statistics
Case Western Reserve University, Cleveland, OH	PhD	06/83	Biostatistics

A. Personal Statement

I am Professor, Department of Medicine and I am Interim Chair of the Biostatistics Shared Resource, Chao Family Comprehensive Cancer Center (CFCCC). I have over 35 years of experience in the design, conduct, and statistical analysis of research studies. I have focused on statistical modeling research that provides insight into biological processes distinguishing between health and disease. In 1993, I was elected a Fellow of the American Statistical Association, in part for "innovative research in biology and medicine". **I have a strong track record of collaboration and publication of research findings and I have a longstanding and successful working relationship Dr. BenMohamed.** For this project, I will supervise analysis of data for the development of a multi-epitope, pan-Coronavirus vaccine. I will assist with the determination of appropriate statistical methodology, performance of statistical analyses, provision of detailed descriptive and analytic reports, and collaboration on abstract and manuscript preparation. I look forward to collaborating with Dr. BenMohamed and colleagues on this unique project.

B. Positions and Honors

Positions and Employment

1976-79 Research Biostatistician, Department of Biometry, Case Western Reserve University
1979-80 Research Officer, Department of Haematology, Welsh National School of Medicine
1980-83 Research Biostatistician, Department of Biometry, Case Western Reserve University
1983-84 Senior Instructor, Department of Biometry and Department of Medicine (Cleveland Metropolitan General Hospital), Case Western Reserve University
1984-86 Assistant Professor, Department of Biometry and Department of Medicine (Cleveland Metropolitan General Hospital), Case Western Reserve University
1986-87 Assistant Professor, Department of Mathematics, Minnesota State University Moorhead
1987-92 Associate Professor, Department of Mathematics, Minnesota State University Moorhead
1992-98 Professor, Department of Mathematics, Minnesota State University Moorhead
1998-2019 Professor of Medicine (Epidemiology) and Director of Biostatistics (Chao Family Comprehensive Cancer Center), University of California, Irvine
2008-2019 Vice Chair for Academic Affairs, Department of Epidemiology, University of California, Irvine
2019-present Professor, Department of Medicine, School of Medicine and Director of Biostatistics (Chao Family Comprehensive Cancer Center), University of California, Irvine

Other Experience and Professional Memberships

1984-2002 International Committee for Standardization in Hematology (Cytometry), Statistical Consultant
1990, 1999 National Science Foundation, Division of Mathematical Sciences, Grant Review Panel
1994, 2000-04 National Institutes of Health, Statistical Reviewer, Hematology Study Section, CSR
2001-2004 Veterans Health Administration, Member, Epidemiology Merit Review Subcommittee

2005-2006	NIH, Ad-hoc Reviewer, NCI Clinical Oncology Study Section
2006	NIH, NCI Initial Review, NCI-A RTRB-H (L1), Subcommittee A – Cancer Centers
2007	NIH Ad-hoc Reviewer, Subcommittee 1-Career Development
2007-2011	NIH, Member, NCI Clinical Oncology (CONC) Study Section
2012	NCI, Reviewer, SPORE in Breast, Endometrial, and Skin Cancers, ZCA1 RPRB-0 M1 P
2013	NCI Oncology 2 - Translational Clinical Integrated Review Group
2014	NCI, Reviewer, P01 Special Emphasis Panel III, ZCA1 RPRB-0 (J1)
2015	NCI, Reviewer, Special Emphasis Panel, ZCA1 PCRB-C (M1) R
2016	NCI Specialized Programs of Research Excellence (SPORE) Review Group
2016	NCI, Chair of Omnibus SEP16 R03 & R21 Review Group, 2016/05 ZCA1 PCRB-C (M1) S
2016	NCI Specialized Programs of Research Excellence (SPORE) Review Group
2018	NCI Specialized Programs of Research Excellence (SPORE) Review Groups
2019	NIH Center for Scientific Review Special Emphasis Panel, ZRG1 EMNR-G (02) M
2020	NIH/NCI CISNET ZCA1 SRB-T M3 Review Group

Honors

1983-84	American Heart Association Research Fellowship
1985	Visiting Scientific Officer, University of Wales College of Medicine, United Kingdom
1986-present	Fellow, Royal Statistical Society
1991	Senior Honorary Research Fellowship, University of Glasgow, United Kingdom
1993	Phi Kappa Phi Honor Society
1993-present	Fellow, American Statistical Association
1994-1995	Raybould Visiting Fellowship, Dept. of Mathematics, Univ. of Queensland, Brisbane, Australia
1995	Senior International Fellowship awarded by the NIH Fogarty International Center
1996	University Dean's Council Nominee, 1997 US Professors of the Year Program, Carnegie Foundation for the Advancement of Teaching
2004	American Statistical Association Service Award, Council of Chapters
2013	Clinical and Translational Science (ICTS) Interdisciplinary Team Science Award, Athena Breast Health Network Program, University of California, Irvine
2014	"Best of ASH" award, 56th meeting of the American Society of Hematology, Dec. 5-9, 2015
2017	Elected member, International Statistics Institute
2017	Received Albert Marquis Lifetime Achievement Award

C. Contributions to Science

1. **Collaborative Research in Cancer**. My collaborative efforts in optical and magnetic imaging are illustrated by my participation as a co-investigator and lead biostatistician for multiple grants. I have co-authored publications resulting from studies of dynamic contrast-enhanced magnetic resonance imaging as a clinical imaging modality for the detection, diagnosis, and treatment of breast lesions. As an example, I supervised statistical modeling using generalized estimating equations (GEE) models that incorporated therapy response, treatment regimen, measurement day, and interaction terms to assess the outcomes of oxyhemoglobin, deoxyhemoglobin, water, and lipid. The results showed that functional hemodynamic and metabolic information acquired using a noninvasive optical imaging method on the first day after neoadjuvant chemotherapy treatment can discriminate nonresponding from responding patients. As Director of the Data Coordinating Center for NIH/NCI grant R01 CA88078-01 (F.L. Meyskens, P.I.), I provided analyses and interpretation of data from the landmark study that demonstrated that recurrent adenomatous polyps can be markedly reduced by a combination of low oral doses of difluoromethylornithine and sulindac and with few side effects.
   a. **McLaren CE**, Fujikawa-Brooks S, Chen W-P, Gillen DL, Pelot D. Gerner EW, Meyskens FL. Longitudinal assessment of air conduction audiograms in a phase III clinical trial of DFMO and sulindac for prevention of sporadic colorectal adenomas. Cancer Prev Res 1:514-521, 2008. PMCID:PMC2702261.
   b. **McLaren CE**, Chen W-P, Nie K, Su M-Y. Prediction of malignant breast lesions from MRI features: a comparison of artificial neural network and logistic regression techniques. Acad Radiol 16(7):842-51, 2009. PMCID: PMC2832583
   c. O'Sullivan TD, Leproux A, Chen JH, Bahri S, Matlock A, Roblyer D, **McLaren CE**, Chen WP, Cerussi AE, Su MY, Tromberg BJ. Optical imaging correlates with magnetic resonance imaging breast density

and reveals composition changes during neoadjuvant chemotherapy. Breast Cancer Res 15(1):R14, 2013. PMCID: PMC3672664.

2. **Hemochromatosis and Iron Overload**. Hemochromatosis is a hereditary disease in which affected persons suffer excessive dietary iron absorption and may lead to complications such as liver cirrhosis, hepatocellular carcinoma, heart failure, diabetes, arthritis, and impotence. I have 24 years of experience working on hematological studies and have published methodological and applied papers related to hemochromotosis, iron overload, and measures of iron status. As Principal Investigator of a Field Center for the Hemochromatosis and Iron Overload Screening (HEIRS) Study, I was lead author on the initial paper describing the overall study design. I supervised enrollment of 20,400 participants at the University of California, Irvine. Based on data from 99,711 participants, we found that the C282Y (substitution of tyrosine for cysteine at amino acid 282) mutation of the *HFE* gene is most common in whites and is accompanied by elevations on iron measures. As a co-investigator for The Melbourne Collaborative Cohort Study, I was co-author of papers describing results from the prospective cohort in which participants born in Australia, New Zealand, the United Kingdom, or Ireland (n=28,509) were genotyped for the *HFE* C282Y variant. Iron-overload-related disease developed in a substantial proportion of C282Y homozygous men. *HFE* C282Y homozygotes have twice the risk of colorectal and breast cancer compared with those individuals without the C282Y variant.
   a. **McLaren CE**, Barton JC, Adams PC, Harris EL, Acton RT, Press N, Reboussin DM, McLaren GD, Sholinsky P, Walker AP, Gordeuk VR, Leiendecker-Foster C, Dawkins FW, Eckfeldt JH, Mellen BG, Speechley M, Thomson E for the Hemochromatosis and Iron Overload Study Research Investigators. Hemochromatosis and iron overload screening (HEIRS) Study Design for an Evaluation of 100,000 primary care-based adults. The Am J Med Sci 325:53-62, 2003. PMID: 12589228..
   b. **McLaren CE**, Gordeuk VR, Chen WP, Barton JC, Acton RT, Speechley M, Castro O, Adams PC, Snively BM, Harris EL, Reboussin DM, McLachlan GJ, Bean R. Bivariate mixture modeling of transferrin saturation and serum ferritin concentration in Asians, African Americans, Hispanics, and Whites in the Hemochromatosis and Iron Overload Screening (HEIRS) Study. Trans Res 151(2):97-109, 2008. PMCID: PMC3785302.
   c. Osborne NJ, Gurrin LC, Allen KJ, Constantine CC, Delatycki MB, **McLaren CE**, Gertig DM, Anderson GJ, Olynyk JK, Powell LW, Hopper JL, Giles GG, English DR. HFE C282Y homozygotes are at increased risk of breast and colorectal cancer. Hepatology 51(4):1311-8, 2009. PMCID: PMC3815603.
3. **Genetic Components of Iron Status**. As PI **OF** NIH grant R01-HL083328-01A1, “Iron Status: A Pathway Analysis in Multiple Ethnicities”, I led a multi-center project to study the heritability of serum iron measures, determine single nucleotide polymorphisms (SNPs) and haplotypes in key genes involved in systemic iron metabolism pathways, identify potential cases of iron deficiency and controls, and study the association between the presence of iron deficiency and haplotypes in the selected candidate genes. Heritability is the proportion of observed variation in a trait among individuals in a population that is attributable to hereditary factors. Participants (N=942) were 77% Caucasians, 10% Asians, 8% Hispanics, and 5% other race/ethnicities. We found that serum iron measures have significant heritability components, after excluding known genetic and nongenetic sources of variation**.** Subsequently, we performed a genome-wide association study (GWAS) using DNA collected from participants in the HEIRS Study to identify new genomic locations associated with iron deficiency. Replication analyses were performed in a sample of veterans screened at a US Veterans Affairs (VA) medical center. The joint analysis of the HEIRS and VA samples revealed strong associations between rs2698530 on chr. 2p14 and iron status outcomes, confirming a previously-described *TF* polymorphism and implicating one potential new locus as a target for gene identification**.** A follow-up study of white, African-American, Hispanic, and Asian HEIRS participants analyzed the association between SNPs and eight iron-related outcomes. Three chromosomal regions showed association across multiple populations, including SNPs in the *TF* and *TMPRSS6* genes, and on chromosome 18q21. A novel SNP rs1421312 in *TMPRSS6* was associated with serum iron in whites ($P=3.7x10^{-6}$) and replicated in African Americans (P = 0.0012). Our results confirmed known associations with iron measures and gave unique evidence of their role in different ethnicities, suggesting origins in a common founder. I am currently the PI of a separate multi-site NIH grant 1R24 DK099846-01A1, “Genetic Modifiers of Iron Status in Hemochromatosis *HFE* C282Y Homozygotes”. We hypothesized that variants of genes other than *HFE* and those previously associated with hemochromatosis and iron overload phenotypes are involved in the regulation of iron metabolism and modulate expression of iron overload in *HFE* C282Y homozygotes. We studied *HFE* C282Y homozygotes at the extremes of phenotypic

expression and determined that *GNPAT* p.D519G is associated with a high-iron phenotype in *HFE* C282Y homozygotes and may participate in hepcidin regulation.

a. **McLaren CE**, Barton JC, Eckfeldt JH, McLaren GD, Acton RT, Adams PC, Henkin LF, Gordeuk VR, Vulpe CD, Harris EL, Harrison BW, Reiss JA, Snively BM. Heritability of Serum Iron Measures in the Hemochromatosis and Iron Overload Screening (HEIRS) Family Study, Am J Hematol 85(2):101-5, 2010**.** PMCID: PMC3816512.
b. **McLaren CE**, Garner CP, Constantine CC, McLachlan S, Vulpe CD, Snivelely BM, Gordeuk VR, Nickerson DA, Cook JD, Leiendecker-Foster C, Beckman KB, Eckfeldt JH, Barcellos LF, Murray JA, Adams PC, Acton RT, Killeen AA, McLaren GD. James D. Genome-wide association study identifies genetic loci associated with iron deficiency. PLoS ONE 6(3):e17390, 2011. PMCID: PMC3069025.
c. **McLaren CE**, McLachlan S, Garner CP, Vulpe CD, Gordeuk VR, Eckfeldt JH, Adams PC, Acton RT, Murray JA, Leiendecker-Foster C, Snively BM, Barcellos LF, Cook JD, McLaren GD. Associationbetween single nucleotide polymorphisms in iron-related genes and iron status in multiethnic populations. PLoS One 7(6):e38339, 2012. PMCID: PMC3382217.
d. **McLaren CE**, Emond MJ, Subramaniam N, Phatak PD, Barton JC, Adams PC, Goh JB, McDonald CJ, Powell LW, Gurrin LC, Allen KJ, Nickerson DA, Louie T, Ramm, GA, Anderson GJ, McLaren GD. Exome sequencing in HFE C282Y homozygous men with extreme phenotypes identifies a GNPAvariant associated with severe iron overload. Hepatology 62(2):429-439, 2015**.** PMCID: PMC450823.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/christine.mclaren.1/bibliography/44197942/public/?sort=date&direction=descending

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

1 R21 HL145232-01 CE McLaren (PI) 09/15/18-08/31/20
NIH/NHLBI
“Modulation of Iron Overload by Hepcidin and Erythroferrone”
This research will conduct a collaborative study to characterize the utility of serum hepcidin concentration and erythroferrone in identifying hemochromatosis patients who are at greatest risk of developing severe iron overload.
Role: PI

2 P30 CA 062203-20, Van Etten, R. (PI) 09/11/97-01/31/21
NIH/NCI
“Cancer Center Support Grant”
The Cancer Center Support Grant provides support for administration and infrastructure for the UC Irvine Chao Family Comprehensive Cancer Center. Dr. McLaren is co-Leader of the Program in Cancer Control and Interim Interim Director of the Biostatistics Shared Resource.
Role: Co-Investigator

5 R01 EY 026103-02 BenMohamed (PI) 08/01/16-7/31/20
NIH/EYI
“Mechanisms of CD8+ T Cell Dynamics in Recurrent Ocular Herpetic Disease”
This is mechanistic and translational preclinical research of recurrent ocular herpes disease, caused by HSV-1 infection, designed to develop a clinical T-cell based immunotherapy against recurrent ocular herpes.
Role: Co-investigator

Completed Research Support (selected)

[redacted]

Role: Co-investigator

5 R24 DK 099846-03 CE McLaren/GD McLaren (PIs) 09/01/14-06/31/19
NIH/NIDDK
“Genetic Modifiers of Iron Status in Hemochromatosis HFE C282Y Homozygotes”
This research is to conduct a collaborative study that will answer the question, "What role do genetic modifiers play in determining iron accumulation in persons homozygous for the HFE C282Y genotype?"
Role: PI

5 DP7 OD 020321-04 Fruman (PI) 09/18/14-08/31/19
NIH/OD
“UCI-GPS: UC Irvine Graduate Professional Success”
This is a campus-wide effort at UC Irvine to broaden the training of biomedical PhD students and postdoctoral fellows and to encourage students and postdoctoral fellows to prepare for a variety of career options.
Role: Co-Investigator

5 R01 CA 195466-02 Tromberg (PI), Kelly (PI) 03/01/16-02/28/19
NIH/NCI
“Quantitative multiphoton microscopy for non-invasive diagnosis of melanoma”
This study will allow us to acquire sufficient clinical data to evaluate the ability of *in vivo* multiphoton microscopy (MPM) to provide quantitative optical imaging endpoints with high predictive power for non-invasive label-free diagnosis of pigmented lesions suspected of melanoma.
Role: Co-Investigator

1R21 CA166839-01A1 (M. Lilly and Z. Zi, MPI) 09/01/13-08/31/15
“Phase 1 bioassay-guided Trial of Lycopene and Docetaxel for Prostate Cancer”
This research will perform a Phase I trial of lycopene in combination with docetaxel as first-line chemo-therapy for patients with castration-resistant prostate cancer.
Role: Co-investigator

1R21 CA170955-01A1 (M-Y Su, PI) 01/15/13–01/14/15
“Volume and Morphology of Fibroglandular Tissue for Breast Cancer Risk”
This project will evaluate the role of MRI-based density parameters, including the volume and the morphology of the fibroglandular tissue, and build a risk prediction model using a case-control study design.
Role: Co-investigator

5 R01 CA 127927-10 Su (PI) 04/01/07-07/31/19
NIH/NC
“Predicting Neoadjuvant Chemo Response/Prognosis Using Imaging Biomarkers”
This project will investigate the role of imaging markers measured by MRI and breast-scintigraphic imaging for predicting the response of breast cancer patients undergoing neoadjuvant chemotherapy (NAC).
Role: Co-investigator

5 R01EY024618-03 BenMohamed (PI) 09/03/14-08/31/18
NIH/NEI
“Blockade of T-cell Co-Inhibitory Pathways and Immunotherapy to Prevent Ocular Herpes”
The goals of this translational project are to understand the T-cell co-inhibitory dependent mechanisms used by HSV-1 to evade CD8+ T cell immunosurveillance and to devise a novel T cell-based immunotherapy.
Role: Co-investigator

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: James V. Jester

eRA COMMONS USER NAME (credential, e.g., agency login): JJESTER

POSITION TITLE: Professor of Ophthalmology and Biomedical Engineering

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Southern California, L.A., CA	B.S.	06/1972	Biology
University of Southern California, L.A., CA	Ph.D.	06/1978	Exp. Pathology
Estelle Doheny Eye Foundation, L.A., CA	PostDoc	07/1982	Ocular Pathology
National Eye Institute, Bethesda, MD	PostDoc	07/1983	Exp. Ocular Pathology

A. Personal Statement

I am an experimental pathologist with a major interest in understanding surface diseases. A major focus of my work has been on developing and evaluating novel imaging modalities for studying structure and cell function. I was involved in developing the first ophthalmic in vivo confocal microscope and I am now using non-linear optical microscopy to evaluate structure and function in situ and ex vivo. We have also recently developed a novel Immunofluorescent Computed Tomography (ICT) method for 3-dimensional reconstruction of tissue that combines NLO imaging with immunocytochemistry to quantitatively and volumetrically assess cell and protein distribution.

[redacted]

1. Parfitt GJ, Xie Y, Reid KM, Dervillez X, Brown DJ, Jester JV: A novel immunofluorescent computed tomography (ICT) method to localise and quantify multiple antigens in large tissue volumes at high resolution. PLosOne 7:e53245, 2012.
2.
3. [redacted]

4. [redacted]

B. Positions and Honors

1974 - 1978	Hugh Edmundson Research Fellow, Dept. of Pathology USC Medical Center, Los Angeles
1981 - 1982	Instructor, Dept. of Ophthalmology & Pathology, USC/Los Angeles County Medical Center, Los Angeles
1982 - 1986	Asst. Prof., Dept. of Ophthalmology & Pathology, USC/Los Angeles County Medical Center, Los Angeles
1986 - 1991	Associate Professor of Ophthalmology & Pathology, Dept. of Ophthalmology/Center for Sight, Georgetown University Medical Center, Washington, DC
1991 - 2004	Professor of Ophthalmology, University of Texas, Southwestern Medical College, Dallas, Texas.
2004 – present	Professor of Ophthalmology and Biomedical Engineering, University of California, Irvine, Irvine, California.
2007 – present	Jack H. Skirball Endowed Chair

Membership on Federal Government Advisory Committees

1989-1991	Ad hoc grant reviewer for NIH VIS A Study Section
1989-1991	Member of Special Study Section -2 for Small Business Innovative Research (SBIR)
1997-1998	Member of the Peer Review Panel on Photorefractive Keratectomy Research for the US Army Medical Research and Materiel Command.
2002-2004	Ad hoc grant reviewer for NIH VIS A Study Section
2004-present	Member of NIH/NEI Anterior Eye Diseases Study Panel
2009	Member of ICCVAM/NICEATM Regulatory Advisory Panel.
2012	Member of the NIH, Neuroscience and Ophthalmic Imaging Technologies Study Section.
2012	Member, Department of Defense, Vision Research Panel Review, American Institute of Biological Sciences.

Awards

1981	Fight for Sight Research Award.
1986	Research Manpower Award, Research to Prevent Blindness, Inc., New York, NY.
1994	Senior Scientist Award, Research to Prevent Blindness, Inc., New York, NY.
2003	2nd Senior Scientist Award, Research to Prevent Blindness, Inc., New York, NY.
2009	ARVO Gold Fellow
2010	Founders Award, Wavefront & Presbyopic Refractive Corrections.
2013	Career Achievement Award, Ocular Toxicology Specialty Section, San Antonio, Texas, March 13, 2013
2017	Thygeson Lecture, Ocular Microbiology and Immunology Group, New Orleans, November 10, 2017.

C. Contribution to Science

1. My laboratory was to first to develop a [redacted] of meibomian gland dysfunction (MGD) and establish a link between hyperkeratinization and ductal plugging of the meibomian gland leading to an experimental model of MGD. As part of this work, we published a novel infrared photography approach to documenting changes in the meibomian gland that today has been modified by others to assess MGD in patients with Dry Eye. Through collaboration with Dr. William Mathers, we later showed that loss of meibomian glands led to increased tear osmolarity and the development of signs and symptoms of Dry Eye. Today, it is widely recognized the MGD is a major cause of Dry Eye disease and is the most common complaint of patients visiting optometric and ophthalmic practices. More recently we have established a [redacted]

of age-related MGD that develops dropout of meibomian glands similar to that observed in older Dry Eye patients that does not involve gland hyper-keratinization (1a,1b), suggesting that meibomian gland cell renewal may play a role in the development evaporative dry eye associated with MG dropout. Towards investigating this theory, we have recently identified and quantified label-retaining cells in the [redacted] meibomian glands and shown that environmental stress leads to up-regulation of cell proliferation (1c). Importantly, hyperproliferation of the meibomian gland may also be associated with direct changes in the quality of the meibomian gland lipid and not hyperkeratinization as reviewed in a recent paper (1d).

1a) Nien CH, Massei S, Lin G, Nabavi C, Tao J, Brown DJ, Paugh JR, Jester JV: Effects of age and dysfunction on human meibomian glands. Arch Ophthalmol 129, 462-469, 2011. PMCID: in progress

[redacted]

1c) Parfitt GJ, Lewis P, Young RD, Richardson A, Lyons JG, Di Girolamo N, Jester JV: Renewal of holocrine meibomian glands by label-retaining, uni-potent epithelial progenitors. Stem Cell Reports 7:399-410, 2016.

1d) Hwang HS, Parfitt GJ, Brown DJ, Jester JV: Meibocyte differentiation and renewal: Insights into novel mechanisms of meibomian gland dysfunction (MGD). Exp Eye Res 163:37-45, 2017.

2. Early my career I was recruited to Georgetown University to help in the development of an in vivo confocal microscope for evaluating corneal cell biology in [redacted] and human subjects. A development team that I helped assemble included Dr. Dwight Cavanagh as a clinician scientist, Dr. Matt Petroll, a Biomedical Engineer with expertise in digital image processing, and myself. Some of the first high-resolution images of living cells using the microscope we developed were published in 1991 (2a), which showed the potential of this new microscopic paradigm for use in clinical diagnosis and treatment of corneal disease (2b). Later we developed novel quantitative approaches to measuring corneal sub-layer thickness using the in vivo confocal microscope (2c), which proved valuable in assessing the response of the cornea to new refractive surgical procedures, particularly photorefractive keratectomy (2d). Today, in vivo confocal microscopy is widely recognized as an important

2a) Jester JV, Petroll WM, Andrews P, Cavanagh HD, Lemp MA: In vivo confocal microscopy. J Elect Micros Tech 18:50-60, 1991.

2b) Cavanagh HD, Petroll WM, Alizadeh H, He Y-G, McCulley JP, Jester JV: Clinical and diagnostic use of in vivo confocal microscopy in patients with corneal disease. Ophthalmol 100: 1444-1454, 1993.

2c) Li H-F, Petroll WM, Maurer JK, Cavanagh HD, Jester JV: Epithelial and corneal thickness measurements by in vivo confocal microscope through focusing (CMTF). Curr Eye Res 16:214-221, 1997.

2d) Moller-Pedersen T, Cavanagh HD, Petroll WM, Jester JV: Stromal wound healing explains refractive instability and haze development after photorefractive keratectomy. A one-year confocal microscopic study. Ophthalmology 107:1235-1245, 2000.

3. Prior to my studies of corneal wound healing, it was generally thought that corneal wounds did not undergo wound contraction similar to skin. My laboratory was the first to establish that corneal wound fibroblasts developed contractile and ultrastructural features consistent with skin myofibroblasts (3a). My laboratory was also to first to establish a serum-free in vitro culture system that maintained the corneal keratocyte phenotype, and showed that the wound cytokine, TGFß, induced expression of α-smooth muscle actin, the biomarker for myofibroblast differentiation (3b). [redacted]

3a) Jester J.V., Rodrigues, M.M., Herman, I.M.: Characterization of avascular corneal wound healing fibroblast. New insights into the myofibroblast. Am. J. Pathol. 127:140-148, 1987.

3b) Jester JV, Barry PA, Cavanagh HD, Petroll WM: Induction of □-smooth muscle actin (□-SM) expression and myofibroblast transformation in cultured keratocytes. Cornea 15:505-516, 1996.

3c) Moller-Pedersen T, Petroll WM, Cavanagh HD, Jester JV: Neutralizing antibody to TGF□ modulates stromal fibrosis but not regression of photoablative effect following PRK. Curr Eye Res 17:736-747, 1998.
3d) Jester JV: Corneal crystallins and the development of cellular transparency. Sem Cell & Devel Biol 19:82-93, 2008.

4. My more recent work has focused on using non-linear optical imaging of second harmonic generated signals (NLO-SHG) to evaluate corneal collagen organization. Using this non-invasive imaging paradigm we were the first to show that NLO-SHG can be used to detect differences in the lamellar organization of collagen in Keratoconus patients compared to normal corneas, which involved the loss of lamellae that inserted into the anterior limiting lamina Bowman's layer (4a). To explore in more depth the significance to these differences, we developed a high-resolution macroscopic approach to imaging the corneal stroma using NLO-SHG that allow for the tracking of single collagen lamellae throughout the length and depth of the cornea (4b). In these studies we showed that the normal human cornea contained 'transverse' collagen lamellae that intertwined with other collagen lamellae and inserted into Bowman's layer. Importantly, these transverse lamellae and lamellar intertwining is highest in the anterior stroma, which we and others have now shown is biomechanically the stiffest region of the cornea. Furthermore, lamellar intertwining and branching seem to be a defining characteristic of corneal development during evolution, with higher vertebrate corneas showing increasing branching combined with increasing mechanical stiffness to control corneal shape (4c). These findings suggest that changes in the macroscopic organization of collagen lead to mechanical weaken and ectasia as observed in Keratoconus. These findings also suggest that mechanical stiffness of the collagen fibers may regulate corneal shape, and that controlling regional corneal stiffness may provide a novel therapeutic strategy for treating refractive errors of the cornea without removal of corneal tissue. To explore test this hypothesis, we are currently developing an NLO corneal crosslinking approach to regionally change corneal stiffness to treated both Keratoconus and potentially other refractive errors (4d).

4a) Morishige N, Wahlert AJ, Kenney MC, Brown DJ, Kawamoto K, Chikama T-I, Nishida T, Jester JV: Second Harmonic Imaging Microscopy of Normal Human and Keratoconus Cornea. Invest Ophthalmol Vis Sci 48: 1087-1094, 2007.
4b) Jester JV, Winkler M, Jester BE, Nien C, Chai D, Brown DJ: Evaluating corneal collagen organization using high resolution non linear optical (NLO) macroscopy. Eye & Contact Lens 36:260-264, 2010.
4c) Koudouna E, Winkler M, Mikula E, Juhasz T, Brown DJ, Jester JV: Evolution of the vertebrate corneal stroma. Prog Ret Eye Res 2018 Feb1, doi: 10..1016/jpreteyeres.2018.01.002.
4d) [redacted]

Complete List of Published Work in MyBibliography:

http://www.ncbi.nlm.nih.gov/sites/myncbi/james.jester.1/bibliograpahy/41149116/public/?sort=date&direction=descending

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D. Research Support

Ongoing Research Support

R01 EY021510 Jester (PI) 09/30/2011 to 08/31/2020
Age-Related Meibomian Gland Dysfunction
The specific aims of this project is to evaluate the effects of age on meibomian gland functions and signal transduction by the lipid sensitive nuclear receptor, peroxisome proliferator-activated receptor-γ (PPARγ)
Role: PI

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: **Pearlman, Eric**

eRA COMMONS USER NAME: **EPEARLMAN**

POSITION TITLE: **Professor**

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Glasgow, Scotland	B.S.	1978	Parasitology
Hebrew University of Jerusalem, Israel	M.S.	1981	Microbiology
University of Texas, San Antonio, TX	Ph.D.	1988	Microbiology
Case Western Reserve University (CWRU), Cleveland OH	Post-doctoral Fellow	1992	Immunology

A. Personal Statement.

My lab and Dr. BenMohamed Labs are adjacent to each other and have collaborated over 4 years. We recently co-senior authors on a recent study on the role of inflammasomes in HSV-1 keratitis (*Frontiers in Immunology*, *2019*). For this project, I will with designing and analyzing tissue-targeted immune checkpoint experiments as described in Aim 2.

In 2006, following an outbreak of contact lens related fungal corneal infections in the USA, we initiated studies on *Fusarium* and *Aspergillus* keratitis, which are major causes of corneal blindness in developing countries. NEI funding in 2008 for murine studies allowed us to identify C-type lectins Dectin-1 and Dectin-2 and IL-17A and IL-1β as major players in innate immunity, and fungal anti-oxidants, and iron and zinc scavengers as important virulence factors (*PLoS Pathogens 2010, 2013, J. Clin Invest 2012, Nat Immunol 2014, J. Immunol 2014, 2016, 2018,*). An Alcon research award in 2010 allowed me to establish a collaboration with the Aravind Eye Hospital in Tamil Nadu, India to examine bacterial and fungal keratitis in infected patients (*J. Infect Dis. 2011, 2015, PLoS One 2013).*

The bacterial keratitis project has since focused on the role of neutrophils as a major source of the pro-inflammatory cytokine IL-1β. We reported that neutrophils have a functional NLRP3 inflammasome that is activated by *Streptococcus pneumoniae* pneumolysin or ATP / P2X7R interactions to mediate caspase-1 processing of IL-1β to the bioactive form *(J. Immunol 2015, Nat. Commun 2016)*. We also found that caspase-1 cleaves the pore-forming protein Gasdermin D in neutrophils and is required for of IL-1β release; however in contrast to macrophages, neutrophils do not undergo pyroptotic cell death.

B. Positions and Honors

Positions and Employment

1994-2000	Assistant Professor, Departments of Medicine and Ophthalmology, Case Western Reserve University (CWRU), Cleveland, OH
2000-2002	Associate Professor, Departments of Medicine and Ophthalmology, CWRU, Cleveland, OH
2002-2004	Associate Professor, Center for Global Health & Diseases and Department of Ophthalmology
2004-2014	Professor, Department of Ophthalmology, CWRU, Cleveland, OH
2004-2014	Director of Research, Department of Ophthalmology and Visual Sciences, CWRU
2015	Director of the Institute for Immunology, University of California, Irvine
2015	Chancellor's Professor, Departments of Ophthalmology, Physiology and Biophysics, UCI

Other Experience and Professional Memberships

2008-2012	Permanent member, Anterior Eye Diseases study section, National Eye Institute
2008-present	Ad hoc member, P-30 core grant reviews, National Eye Institute
2013-present	Ad hoc member, NEI T32, T35, and K12 study sections
2013	Ad hoc member, Disease and Pathogenesis of Visual Sciences special emphasis panel
2019	Editorial Board, Frontiers in Immunology
2019	Ad hoc member, NIAID Innate Immunity and Inflammation study section

Honors

1997	Burroughs Wellcome Foundation New Investigator Award
2004	University of Western Australia Raine Foundation Visiting Professorship
2006	Research to Prevent Blindness Foundation: Senior Investigator Award
2010	Alcon Research Institute award
2011-2014	Page-Reinhart Endowed Professorship, Case Western Reserve University
2015	Chancellor's Professor, UC Irvine

C. Contributions to Science

i) Pathogenesis of *Pseudomonas aeruginosa* corneal infections: **EY14362** was first awarded in 2004 with the goal of understanding the role of Toll Like Receptors (TLR) in corneal inflammation. In the first funding period, we characterized TLR signaling in the corneal epithelial cells and in infiltrating macrophages and neutrophils, resulting in multiple papers in the *Journal of Biological Chemistry, J. Immunol, J. Leukocyte Biology,* and *IOVS*. Subsequent studies with Arne Rietsch at CWRU characterized TLR signaling in *Pseudomonas aeruginosa* keratitis, which we reported in 2010 in *J Immunol* (PMC3392180). We also identified the ADPRT region of ExoS and ExoT as the essential *P. aeruginosa* type III secretion (T3SS) virulence factors in keratitis (*J. Immunol 2012.* PMC3273577**)**. We continued this collaboration after I moved to UCI, demonstrating that ExoS enhances *P. aeruginosa* survival in human neutrophils by inhibiting ROS production by ADP ribosylating Ras and thereby blocking NADPH oxidase assembly (*Cell Host and Microbe 2017*).

Our studies in India showed that IL-1β gene expression was elevated in human corneal ulcers caused by bacteria, which were mostly comprised of neutrophils *(PLoS One 2013,* PMC3672173*)*. Using a murine model of *P. aeruginosa* keratitis, we showed that IL-1β plays an essential role in bacterial clearance, and that neutrophils were the predominant source of cleaved, bioactive IL-1β.

1. Vareechon C, S.E. Zmina, M. Karmakar, **E. Pearlman**, and A. Rietsch. (2017) Pseudomonas aeruginosa Effector ExoS Inhibits ROS Production in Human Neutrophils. ***Cell Host & Microbe*** 21: 611-618 e615. PMC5478421.

2. Karmakar, M., Y. Sun, A. G. Hise, A. Rietsch and **E. Pearlman**. 2012. ***Cutting Edge:*** IL-1β processing during *Pseudomonas aeruginosa* infection is mediated by neutrophil serine proteases and is independent of NLRC4 and Caspase-1. ***J. Immunol*.** 189:4231-4235. PMC3482477
3. Sun, Y., P. Taylor, A. Rietsch and E. Pearlman. 2012. ExoS and ExoT ADP Ribosyltransferase activities mediate *Pseudomonas aeruginosa* keratitis by promoting neutrophil apoptosis and bacterial survival. ***J. Immunol.*** 188(4):1884-95. PMC3273577.
4. Sun, Y. M. Karmakar, S. Roy, R. T. Ramadan, S. R. Williams, S. Howell, C. L. Shive, Y. Han, C. M. Stopford, A. Rietsch and **E. Pearlman**. 2010. TLR4 and TLR5 on corneal macrophages regulate *Pseudomonas aeruginosa* keratitis by signaling through MyD88-dependent and -independent pathways. ***J. Immunol.*** 185:4272-83. PMC3392180

ii) IL-1β processing by neutrophils as in *Streptococcus pneumoniae* corneal infections: Our studies in India also showed that *Strep pneumoniae* clinical isolates from human corneal ulcers all produced pneumolysin *(PLoS One 2013,* PMC3672173*)*. Using a murine model of *Strep pneumoniae* keratitis, we showed that IL-1β plays an essential role in bacterial clearance, and that neutrophils were the predominant source of cleaved, bioactive IL-1β, which was mediated by pneumolysin as signal 2 activation of the NLRP3 inflammasome. We also found that in marked contrast to macrophages, neutrophils release bioactive IL-1β in the absence of pyroptotic cell death. We subsequently showed that

1. Karmakar, M., M. Katsnelson, **G.R. Dubyak**, and **E. Pearlman**. (2016) Neutrophil P2X7 receptors mediate NLRP3 inflammasome-dependent IL-1β secretion in response to ATP. ***Nature Communications***. 15; 7:10555. PMC4756306.
2. Karmakar, M., M. Katsnelson, N.G. Greene, H. A. Malak, Scott Howell, A. G. Hise, A. Camilli, A. Kadioglu, **G. R. Dubyak** and **E. Pearlman**. (2015) Pneumolysin induces K^+ efflux and NLRP3/ Caspase 1 dependent IL-1β processing by neutrophils. ***J. Immunol.*** 194:1763-75. PMC4369676.

iii) Pathogenesis of fungal corneal infections Our [redacted] on fungal keratitis are based on corneal ulcer material, post- transplant corneas, and peripheral blood from patients in southern India (*J. Infect Dis 2015*. In addition to examining the host response to pathogenic *Aspergillus* and *Fusarium* species, we identified fungal antioxidant and iron binding pathways as novel therapeutic approaches for fungal keratitis (*J. Clin Invest 2012; PLoS Path 2013)*. Similarly, we showed that neutrophils use calprotectin (S100A8/A9) to sequester zinc and manganese, and thereby limit hyphal growth in the cornea, and that topical application of atovaquone inhibits hyphal growth in the cornea by the same mechanism (IOVS 2018). Recently, we revealed a role for CR3 rather that NETs in hyphal killing, reported an unexpected role for caspase-11 in IL-1β processing by neutrophils, and found a role for acidic mammalian chitinase in fungal keratitis.

1. Carrion Sde, J., S. Abbondante, H. Clark, and **E. Pearlman**. 2019. Aspergillus fumigatus corneal infection is regulated by chitin synthases and by neutrophil–derived acidic mammalian chitinase *Eur J Immunol.* 10.1002/eji.201847851. PMID: 30903663
2. Sun, Y., S. Abbondante, M. Karmakar, S. de Jesus Carrion, C. Che, A. G. Hise and **E. Pearlman**. 2018. Neutrophil caspase-11 is required for cleavage of caspase-1 and secretion of IL-1β in *Aspergillus fumigatus* infection. Journal of Immunology. 201(9):2767-2775. PMC6200591. (Featured in *In this Issue* as top 10% of papers*)*
3. Clark, H.L., S. Abbondante, M.S. Minns, Y. Sun, E. N. Greenberg, and **E. Pearlman**. 2018. Protein Deiminase 4 (PAD4) and CR3 regulate *Aspergillus fumigatus* and β-glucan – induced neutrophil extracellular trap formation, but hyphal killing is dependent only on CR3. ***Frontiers Immunol.*** 9:1182*.* PMC5986955.
4. Clark, H. L., A. Jhingran, Y. Sun, C. Vareechon, S. de Jesus Carrion, E.P. Skaar, W.J. Chazin, J.A. Calera, T.M. Hohl, and **E. Pearlman.** (2016) Zinc and Manganese Chelation by Neutrophil S100A8/A9 (Calprotectin) Limits Extracellular Aspergillus fumigatus Hyphal Growth and Corneal Infection. ***J Immunol*** 196, 336-44. PMC4684987 (Featured in *In this Issue* as top 10% of papers)

iv) Neutrophils as a source of IL-17A (IL-17): Collaborative studies on *Aspergillus* and *Fusarium* keratitis patients at the Aravind Eye Institute in south India indicated that in addition to T cells, neutrophils appeared to be a source of IL-17 in corneal ulcers and in the peripheral blood (*J. Infect Dis 2011, 2015)*. This was confirmed using [redacted] of fungal keratitis, and identified a role for IL-6, IL-23 and

RORγT in this process. We also found IL-17 producing neutrophils in cystic fibrosis patients undergoing pulmonary exacerbations.

1. Taylor, P. R., S. Roy, E. C. Meszaros, Y. Sun, S. J. Howell, C. J. Malemud, and **E. Pearlman**. 2016. JAK/STAT regulation of *Aspergillus fumigatus* corneal infections and IL-6/23 - stimulated neutrophil elastase and MMP-9 activity. ***J. Leuk. Biol***. 100: 213-222. PMC4946614
2. Taylor, P.R., S. Roy, S.M. Leal, Jr., Y. Sun, S.J. Howell, B.A. Cobb, X. Li and **E. Pearlman**. (2014) Autocrine IL-17A / IL-17RC neutrophil activation in fungal infections is regulated by IL-6, IL-23, RORγ t and Dectin-2. ***Nature Immunology***. 2: 143-151. PMC3972892.
3. Taylor, P. R., S. M. Leal, Jr., Y. Sun, and **E. Pearlman.** 2014**.** Aspergillus and Fusarium corneal infections are regulated by Th17 cells and IL-17 producing neutrophils. ***J. Immunol***. 2014;192:3319-27. PMC4020181.
4. Taylor, P., T. Bonfield, J. Chmiel, and **E. Pearlman**. 2016. Neutrophils from F508del cystic fibrosis patients produce IL-17A and express IL-23 - dependent IL-17RC. ***Clin Immunol.*** 170: 53-60. PMID: 27155366

v) Host response to ocular onchocerciasis (river blindness): *Onchocerca volvulus* is a filarial nematode that is transmitted by blackflies (that breed in rivers). Migration of larvae through the skin and into the eye was a devastating cause of blindness, and continues to be a cause of severe skin infections and blindness in sub-Saharan Africa. As a post-doctoral fellow, I established a murine model to examine the role of T helper cells in host defense (J*. Exp. Med. 1995*), which led to a number of papers characterizing the adaptive immune response in regulating corneal disease. Later, we shifted our focus to innate immune responses to *O. volvulus* in the cornea, and found that the TLR2 signaling pathway was a critical player. Subsequently we showed that TLR2 was responding not to the filarial nematode, but rather to the endosymbiotic Rickettsia-like bacteria *Wolbachia pipiensis*. In collaboration with Mark Taylor and Achim Hoerauf, we published our findings in *Science,* which was broadly covered in *Science* (Hidden Culprits) and in multiple other journals and the mainstream media. Mark Taylor identified the TLR2/6 ligand as the major *Wolbachia* lipopeptide (*J Biol Chem 2009*). After we identified ligand/receptors as major initiators of corneal disease, I chose not to renew the grant, which had been funded by the National Eye Institute from 1993-2008.

1. Tamarozzi F, Halliday A, Gentil K, Hoerauf A, **Pearlman E**, Taylor MJ. 2011. Onchocerciasis: the role of Wolbachia bacterial endosymbionts in parasite biology, disease pathogenesis, and treatment. Clin Microbiol Rev. 24:459-68
2. Turner, J. D., R. S. Langley, K. Johnston, K. Daehnel, L. Ford, B. Wu, M. Graham, F. Sharpley, B. Slatko, **E. Pearlman** and M. J. Taylor. 2009. Filarial Wolbachia lipoprotein stimulates innate and adaptive inflammatory responses through TLR2 and TLR6 and induces disease manifestations of lymphatic filariasis and river blindness. ***J. Biol. Chem***. 284, 22364-22378.
3. Hise, A.G., K.Daehnel, I. Gillette-Ferguson, E. Cho, H. F. McGarry, M. J. Taylor, D. T. Golenbock, K. A. Fitzgerald, J. W. Kazura and **E. Pearlman**. 2007. Innate immune responses to endosymbiotic *Wolbachia* bacteria in *Brugia malayi* and *Onchocerca volvulus* are dependent on TLR2, TLR6, MyD88 and Mal, but not TLR4, TRIF or TRAM. ***J. Immunol***. 178: 1068-1076.
4. Saint André, A. v., N. M. Blackwell, L. R. Hall, A. Hoerauf, N. W. Brattig, L. Volkmann, M. J. Taylor, L. Ford, A. G. Hise, J. H. Lass, E. Diaconu, and E. **Pearlman**. 2002. The Role of Endosymbiotic *Wolbachia* Bacteria in the Pathogenesis of River Blindness. ***Science***. 295:1892-1895.

Complete List of Published Work (120 reports, 29 reviews, 3 book chapters):
https://www.ncbi.nlm.nih.gov/pubmed?term=Pearlman%2C%20Eric%5BAuthor%5D

Patents: I am a named inventor on the following patent applications based on studies from NEI grant EY14362:

1. US 9006210: Toll Like Receptors (TLR) as targets for therapeutic and prophylactic intervention in contact lens associated keratitis and sterile corneal infiltrates
2. US 20080008749: System and Method for delivery of Ceramide Analogs to Inhibit Ocular Inflammation

Additional Information: Research Support

RO1 EY018612 Pearlman (PI) 03/01/08 – 12/31/23
National Eye Institute
Pathogenesis of Fungal Keratitis
[redacted] of fungal keratitis. Studies will also characterize the role of neutrophil extracellular traps (NETs), which can limit hyphal growth, but also have the potential to contribute to tissue damage.
Role: PI (30% effort)
Annual direct costs: $271,517

RO1 EY014362 Pearlman (PI) 12/01/03 – 7/31/23
National Eye Institute
Pathogenesis of Bacterial Keratitis
This project examines the role of IL-1β and inflammasomes in the innate immune response in bacterial keratitis and in response to bacterial products in the cornea
Role: 2019-2023: Co-PI with George Dubyak, CWRU, 10% effort
Annual direct costs: $256,000

NIAID T32 AI060573 Pearlman (PI) 08/18/16 – 07/31/21
Immunology Research Training Grant for UC Irvine
This grant covers the tuition and stipends for 3 pre-doctoral positions (a 4th position is provided by UCI School of Graduate Studies).
Role: PI (5% effort)
Annual direct costs: $110,550

R01 EY030150 (Li-Jun Ma, UMASS, PI) 05/01/19 – 04/30/2024
Identify novel Fusarium virulence factors
Comparative genomics studies focused on plant pathogenic F. oxysporum isolates demonstrated horizontal transfer of supernumerary (SP) chromosomes conveys plant host-specific pathogenicity. A recent study of a F. oxysporum clinical isolate revealed four unique SP chromosomes and confirmed that SP chromosomes can mediate pathogen adaptation to human body conditions, such as higher temperatures and alkaline pH and iron-poor environments. The current proposal capitalizes on our understanding of SP chromosomes that contribute directly to fungal pathogenicity, and will identify pathogenic SP chromosomes, using a high - throughput screening pipeline using transcriptomics, forward/reverse genetics and experimental evolution approaches to identify novel virulence factors.
Role: Co-Investigator (5% effort)
Annual direct costs: $250,000

PR161453 Yee, Albert (PI) 08/01/17 – 07/31/20
US Army Medical Research Acquisition Activity (USAMRAA)
Novel Bandage Contact Lens Against Resistant Fungal Infections with Ocular Drug Delivery
This project will design and evaluate in vitro a novel, multi-functional antifungal material (chitin- chitosan) with both inherent antifungal properties and antifungal drug-releasing characteristics. This project is a proof-of-concept application as a surface for a bandage contact lens.
Role: Co-Investigator (10% effort)
Annual direct costs: $500,000

OMB No. 0925-0001 and 0925-0002 (Rev. 03/2020 Approved Through 02/28/2023)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Lanny Hsieh

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Health Sciences Clinical Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
California Institute of Technology, Pasadena, CA	BS	1995	Biology
New York University School of Medicine, NY, NY	MD	1999	Medicine
University of California, Irvine, CA	Residency	2002	Internal Medicine
University of California, Irvine, CA	Fellowship	2007	Infectious Diseases

A. Personal Statement

I will help Dr. BenMohamed with COVID-19 patients recruitment and identification of symptomatic and asymptomatic patients as described in Aim 1 of this Pan-Coronavirus vaccine R01 proposal.

I have been clinical faculty at UCI Medical center since 2007. My time has been spent in direct patient care, education, and quality improvement. I serve as the Infectious Disease Consult attending 5 months of the year, and serve as Hospitalist attending 2 months of the year. I work closely with Medical Students, Internal Medicine Residents, Infectious Disease Fellows, and Pharmacy Residents. In addition to various lectures, I have been invited to speak at regional meetings. In 2009, I was invited to speak at the UC Irvine Family Medicine Update Course. In March, 2017, I was invited to speak at the UC Irvine 2nd Annual Hematology Symposium. In 2018, I spoke at the Texas Club of Internists (TCI), the Southern California Region II American College of Physicians (ACP) and the UC Irvine Department of Medicine (DOM) conference. I have written book chapters in Antimicrobial Stewardship, and Infectious Diseases and Pregnancy. In 2011, my pilot study on prospective audit of restricted antibiotic utilization provided data demonstrating the effectiveness of antimicrobial stewardship interventions and cost savings that helped provide the impetus to develop a comprehensive antimicrobial stewardship program at UC Irvine Medical Center.

I have worked as an integral part of the UCI Medical Center community. I was the physician champion for Sepsis, which included several ongoing projects (Sepsis Core Measures, Hospital-Acquired Sepsis, and Bundled Payments on Sepsis). I am also the Medical Director for the Clinical Documentation Improvement project. I have been and continue to be an active member of the Antimicrobial Stewardship Sub-committee and the Epidemiology and Infection Prevention Committee. I also served as Member-at-Large on the Medical Executive Committee 2015-2017.

My work as an Infectious Diseases Hospitalist has given me the opportunity to be involved in the various aspects of clinical medicine, teaching, research, leadership, and process improvement. I am currently the clinical lead in the COVID-19 Hospital Incident Command System committee at UC Irvine Medical Center. I am also the PI for the UC Irvine Site in NIAID's multicenter adaptive treatment trial on Remdesivir. I am

involved in several upcoming clinical research projects related to the treatment of COVID-19 in hospitalized patients.

B. Positions and Honors

2002-2005: Physician, Internal Medicine and Family Practice, Alhambra, CA
2007-2013: Health Sciences Assistant Clinical Professor, University of California, Irvine Medical Center
2013-2019: Health Sciences Associate Clinical Professor, University of California, Irvine Medical Center
2019-present: Health Sciences Professor, University of California, Irvine Medical Center

2000-2019: Director of Medical Clerkships, Division of Infectious Diseases
2007-2010: Future Health Professional Club, Faculty Mentor
2007-2011: "Through the Eyes of the Patient – HIV/AIDS", Faculty Advisor
2011-2018: Sepsis Task Force, Medical Director
2013-2016: Inpatient Clinical Documentation / Governance, member
2015-2018: Bundled Payment for Care Improvement, Sepsis, Physician Champion
2015-2017: Medical Executive Committee, Member-at-Large

2011-present: Clinical Documentation Improvement, Medical Director
2015-present: Hospitalist IV Antibiotics Clinic, co-Medical Director
2014-present: Vaccine Advisory Group, Inpatient Physician Champion
2007-present: Epidemiology and Infection Prevention Committee, member
2007-present: Antibiotic Stewardship Subcommittee, member

C. Contributions to Science

PUBLICATIONS:

Journal Articles:

1. Feistner G.J., **Hsieh L.L**., *Metabolites of Erwinia. On the Collision-Activated Fragmentation of Proferrioxamines: Evidence for a Succinimide-Mediated Mechanism*, Journal of the American Society for Mass Spectrometry, 1995 Sep, V6 N9:836-846.

2. Weng R, Foster C, **Hsieh L**, Patel P. *Oral Ulcers Associated with Mycophenolate Mofetil use in a Renal Transplant Recipient*, American Journal of Health-System Pharmacy. 1 April 2011; Vol. 68, No. 7.

3. **Hsieh, L**, Amin, A. Antimicrobial Stewardship: The Role of Hospitalists and the Emergency Department, Current Emergency and Hospital Medicine Reports, DOI: 10.1007/s40138-016-0112-3.

4. Speiser L, **Hsieh L**, Huang SS, Bittencourt C, Fortal D, *Brucellosis Presenting as Cholecystitis: A Case Report and Review of the Literature*, Open Forum Infectious Diseases, Volume 6, Issue 10, October 2019.

5. Ferrey A, Choi G, Hanna RM, Chang Y, Tantisattamo E, Ivaturi K, Park E, Nguyen L, Wang B, Tonthat S, Rhee CM, Reddy U, Lau WL, Huang SS, Gohil S, Amin AN, **Hsieh L**, Cheng TT, Lee RA, Kalantar-Zadeh K. *A Case of Novel Coronavirus Disease 19 in a Chronic Hemodialysis Patient Presenting with Gastroenteritis and Developing Severe Pulmonary Disease*, American Journal of Nephrology, DOI: 10.1159/000507417.

Book Chapters:

1. **Hsieh, L**, Amin, A. *Antibiotic Stewardship: Hospital Strategies to Curb Antibiotic Resistance*, Antibiotic Resistance, Elsevier, 2016.

2. **Hsieh, L**, Watanabe, M. *Infectious Disease and Pregnancy*, OB/GYN Hospitalist Medicine:

Principles and Practice, McGraw-Hill, Jan 2019.

D. Research

NIH/NIAID NCT04280705
HS 2020-5769 University of California, Irvine site Hsieh (PI) 3/2020 – 4/2023
A Multicenter, Adaptive, Randomized Blinded Controlled Trial of the Safety and Efficacy of Investigational Therapeutics for the Treatment of COVID-19 in Hospitalized Adults
Role: PI, UCI Site

HS 2020-5878 Tran (PI) 5/2020-
Expanded Access to Convalescent Plasma for the Treatment of Patients with COVID-19
Role: Co-Investigator

NeuroRx Lee (PI) 5/2020-
RFL-100 (Aviptidil) for the Prevention and Treatment of Acute Lung Injury/Acute Respiratory Distress Syndrome in COVID-19
Role: Sub-Investigator

GAM10-10 Amin (PI) Pending
OctaPharma
Efficacy and Safety of Octagam 10% Therapy in COVID-19 Patients with Severe Disease Progression
Role: Co-Investigator

CSSC-001 Forthal/Amin/Tran (PI) Pending
PEP Protocol: Convalescent Plasma to Stem Coronavirus: A Randomized Controlled Double Blinded Phase 2 Study Comparing the Efficacy and Safety of Human Coronavirus Immune Plasma (HCIP) vs. control (SARS-CoV-2 non-immune plasma) among Adults Exposed to COVID-19STUDY DRUG: MAS825 is an IgG1 mAb (single dose of MAS825/placebo 10mg/kg IV)
Role: Co-Investigator

CSSC-004 Forthal/Amin/Tran (PI) Pending
Convalescent Plasma to Limit Coronavirus Associated Complications: A Randomized, blinded Phase 2 Study Comparing the Efficacy and Safety Human Coronavirus Immune Plasma (HCIP) vs. control (SARS-CoV-2 non-immune plasma) among Symptomatic Adults Positive for SARS-CoV-2
Role: Co-Investigator

PUL-042-501 Amin (PI) Pending
Pulmotech
A Phase 2 Multiple Dose Study to Evaluate the Efficacy and Safety of PUL-042 Inhalation Solution in Reducing the Infection Rate and Progression to COVID-19 in Adults Exposed to SARS-CoV-2
Role: Sub-Investigator

PUL-042-502 Amin (PI) Pending
Pulmotech
A Phase 2 Multiple Dose Study to Evaluate the Efficacy and Safety of PUL-042 Inhalation Solution in Reducing the Severity of COVID-19 in Adults Positive for SARS-CoV-2 Infection
Role: Sub-Investigator

2020-5783 Bota (PI) Pending
Comprehensive Clinical, Imaging and Histological Database for the Study of COVID-19 Infection and Outcomes
Role: Co-Investigator

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Burkhard, Peter

eRA COMMONS USER NAME (credential, e.g., agency login): PETERBURKHARD

POSITION TITLE: CEO

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Biozentrum, University of Basel, Basel, Switzerland	Diploma	1992	Biochemistry
Sandoz Pharma AG, Basel, Switzerland	PhD	1995	Biophysics
Biozentrum, University of Basel, Basel, Switzerland	Postdoc	1998	Structural Biology
Biozentrum, University of Basel, Basel, Switzerland	Habilitation	2001	Structural Biology

A. Personal Statement

My experience and qualifications make me particularly well-suited for the role as co-PI in this HSV nanoparticle vaccine project. The nanoparticles have been invented by me about fifteen years ago. Ever since I have continuously and with great enthusiasm further developed the nanoparticles to make them suitable as a platform for vaccine design. I have analyzed their biophysical and immunological properties in great detail resulting in the production of five vaccine prototypes for four different infectious diseases that all are almost completely protective in animal challenge models. This work resulted in five different patents / patent applications of SAPNs for vaccine design (US8575110, US8546337, EP2766386A1, EP2766386A1, EP17157687.9). I have also advanced our most developed malaria SAPN vaccine up to the stage of clinical trials phase I/IIa, which is planned to be finished in summer (2018). Furthermore, I have founded the company Alpha-O Peptides more than a decade ago. Developing vaccines is the core business of this company. For all those reasons, I think that I am perfectly qualified to be the lead PI at Alpha-O Peptides in this HSV vaccine project. I strive to develop the HSV vaccine to possibly also bring it into clinical trials as quickly as possible. My personal background covering everything from nano-biotechnology to immunology and including all aspects that are important for vaccine design makes me perfectly suited to direct the research of this proposal.

I will collaborate with the principal investigator, Dr. BenMohamed from the UC Irvine on this proposal that is developing the prime pull/vaccine against genital herpes. The scope of work of this R01 grant entitled "***A Novel Prime/Pull Therapeutic Vaccine to Prevent Recurrent Genital Herpes***" is to develop a Self-Assembling Protein Nanoparticles (SAPNs) combined with T-cell attracting chemokines against recurrent genital herpes in [redacted] Self-Assembling Protein Nanoparticles (SAPNs) will be provide UC Irvine during the first 2-years of this project. [redacted]

The following are my most relevant patents / patent applications.

a) US8575110 (2004). "Peptidic Nanoparticles as Drug Delivery and Antigen Display Systems" **P. Burkhard**

b) US 8546337 (2008). "Self-assembling peptide nanoparticles useful as vaccines" **P. Burkhard**
c) WO2015104352 (2014). "Flagellin-containing protein nanoparticles as a vaccine platform" by S.K. Raman, S.M. Paulillo, M. Piazza, C. Kulangara, C. Mittelholzer, and **P. Burkhard**
d) EP17157687.9 (2017). "Self-assembling protein nanoparticles encapsulating immunostimulatory nucleid acids" by S.K. Raman, S.M. Paulillo, C. Kulangara, M. Piazza and **P. Burkhard**

B. Positions and Honors

- 1995 - 1998 Postdoctoral Position at the Biozentrum, University of Basel, CH
- 1998 - 2004 Group leader at the Biozentrum, University of Basel, CH
- 2001 Habilitation, University of Basel, CH
- 2003 Founder of Alpha-O Peptides, AG, Riehen, CH
- 2004 - 2013 Associate Professor, University of Connecticut, CT, USA
- 2013 - 2015 Full Professor, University of Connecticut, CT, USA
- 2015 - 2016 Research Professor, University of Connecticut, CT, USA
- 2003 - CEO of Alpha-O Peptides, AG, Riehen, CH

- 2005 Senior Founding Member of the American Academy of Nanomedicine
- 2006 Fellow of the American Academy of Nanomedicine
- 2010 Tenured faculty position at the University of Connecticut
- 2011 - Editor of the Journal of Nanobiotechnology
- 2011 Director's Award for Faculty Excellence, Polymer Program, University of Connecticut
- 2012 - Editor of Current Bionanotechnology

C. Contribution to Science

1. Protein Structural Analysis for Structure Based Design

DOPA decarboxylase (DDC) is responsible for the synthesis of the key neurotransmitters dopamine and serotonin via decarboxylation of L-3,4-dihydroxyphenylalanine (L-DOPA) and L-5-hydroxytryptophan, respectively. DDC has been implicated in a number of clinic disorders, including Parkinson's disease and hypertension. Peripheral inhibitors of DDC are currently used to treat these diseases. We have solved the X-ray crystal structures of ligand-free DDC and its complex with the anti-Parkinson drug carbiDOPA. The inhibitor is bound to the enzyme by forming a hydrazone linkage with the cofactor, and its catechol ring is deeply buried in the active site cleft. These structures provide the molecular basis for the development of new inhibitors of DDC with better pharmacological characteristics. P. Burkhard et al. (2001) Nature Struct Biol, 8 (11), 963 – 967).

Publication of these DDC structures prompted Rebecca Craven to write the following comments in the Highlights section in Nature Reviews Neuroscience (2002) 2 (12), 855: *The treatment of patients with Parkinson's disease could be greatly improved by the design of more effective inhibitors of this enzyme. This prospect seems increasingly likely, as Burkhard et al. report the crystal structures of ligand-free DCC, and its complex with carbiDOPA. Importantly, on the basis of these structures, the authors were able to suggest ways in which the binding of inhibitors of DCC might be improved. The use of more-potent inhibitors of DCC would allow smaller amounts L-DOPA to be used in alleviating the symptoms of Parkinson's disease; the crystal structures reported by Burkhard et al. offer a way forward in the design of such treatments.*

e) **Burkhard, P.**, Dominici, P., Borri-Voltattorni, C., Jansonius, J.N., and Malashkevich, V.N. Structural insight into Parkinson's disease treatment gained from drug-inhibited DOPA decarboxylase. *Nature Struct Biol*. 2001 Nov;8(11):963-967. PMID: 11685243

f) Meier, M., Janosik, M., Kery, V., Kraus, J. and **Burkhard, P**. Structure of human cystathionine beta-synthase: a unique pyridoxal 5'-phosphate-dependent heme protein. *EMBO J*. 2001 Aug 1;20(15):3910-3916. PMCID: PMC149156

g) Stetefeld, J., Jenny, M., and **Burkhard, P**. Intersubunit signaling in glutamate-1-semialdehyde-aminomutase. *Proc Natl Acad Sci U S A*. 2006 Sep 12;103(37):13688-13693. PMCID: PMC1564225

h) **Burkhard, P**., Rao, G.S., Hohenester, E., Schnackerz, K.D., Cook, P.F. & Jansonius, J.N. Three-dimensional Structure of *O*-acetylserine Sulfhydrylase from Salmonella typhimurium. *J Mol Biol*. 1998;283(1):121-133. PMID: 9761678

2. Structural Design and Analysis of Coiled-coil Proteins

The parallel two-stranded α-helical coiled coil is the most frequently encountered subunit-oligomerization motif in proteins. The simplicity and regularity of this motif have made it an attractive system to explore some of the fundamental principles of protein folding and stability and to test the principles of de novo design. We have solved the X-ray crystal structure of the 18-heptad-repeat α-helical coiled-coil domain of the actin-bundling protein cortexillin I from Dictyostelium discoideum and shown that it is a tightly packed parallel two-stranded α-helical coiled coil. It harbors a distinct 14-residue sequence motif that is essential for coiled-coil formation, and is a prerequisite for the assembly of cortexillin I. The knowledge gained from the structure can be used in the de novo design of α-helical coiled coils for applications such as two-stage drug targeting and delivery systems, and in the design of coiled coils as templates for combinatorial helical libraries in drug discovery and as synthetic carrier molecules. (P. Burkhard et al. (2000). *Structure*, **8**, 223-230.)

Presentation of this structure at the American Crystallographic Association Annual Meeting 1999 in Washington triggered the following Editorial Reprise in *Nature Struct. Biol*., 5, (1998), 762 by Guy Riddihough. *Perhaps the most apposite example was provided by P. Burkhard who reported on the structure determination of the 190 Å long α-helical, two-stranded, right-handed coiled-coil rod domain from cortexillin I. This is the longest structure of a coiled coil reported to date, soundly beating the 39-residue long cFos-cJun bZIP leucine zipper. The rod domain includes a 13-residue 'trigger site' that has been shown to be necessary for coiled coil assembly and, indeed, has been characterized as an autonomous folding unit, suggesting that this is a general feature of coiled coil assembly.*

a) Strelkov, S., Herrmann, H., Geisler, N., Zimbelmann, R., Aebi, U. and **Burkhard, P**. Conserved segments 1A and 2B of the intermediate filament dimer: their atomic structures and role in filament assembly. *EMBO J*. 2002 Mar 15;21(6):1255-1266. PMCID: PMC125921

b) Strelkov, S.V., and **Burkhard, P**. Analysis of alpha-helical coiled coils with the program TWISTER reveals a structural mechanism for stutter compensation. *J Struct Biol*. 2002 Jan-Feb;137(1-2):54-64. PMID: 12064933

c) **Burkhard, P**., Kammerer, R.A., Steinmetz, M.O., Bourenkov, G.P. and Aebi, U. The coiled-coil trigger site of the rod domain of cortexillin I unveils a distinct network of inter- and intra-helical salt-bridges. *Structure*. 2000 Mar 15;8(3):223-230. PMID: 10745004

d) **Burkhard, P**., Meier, M. and Lustig, A. Design of a minimal protein oligomerization domain by a structural approach. *Protein Science*. 2000 Dec;9(12):2294-2301. PMCID: PMC2144530

3. Structural Design of Self-Assembling Protein Nanoparticles (SAPNs)

Artificial particulate systems such as polymeric beads and liposomes are being applied in drug delivery, drug targeting, antigen display, vaccination, and other technologies. We have used computer modeling to design a novel type of self-assembling protein nanoparticles (SAPNs) composed of proteins as building blocks. We describe the structure-based design of a novel type of nanoparticles with regular polyhedral symmetry and a diameter of about 16 nm, which self-assembles from single protein chains. Each protein chain is composed of two coiled coil oligomerization domains with different oligomerization states joined by a short linker segment. In aqueous solution the proteins form nanoparticles of about 20 nm diameter. Such protein nanoparticles are ideally suited for medical applications such as drug targeting and drug delivery systems, as imaging devices, or they may be used for repetitive antigen display.

a) Raman, S.K., Machaidze, G., Lustig, A., Aebi, U. and **Burkhard, P**. Structure-based design of peptides that self-assemble into regular polyhedral nanoparticles. *Nanomedicine*. 2006 Jun;2(2):95-102. PMID: 17292121

b) Pimentel T.A., Yan Z, Jeffers S.A., Holmes K.V., Hodges R.S. and **Burkhard P**. Peptide nanoparticles as novel immunogens: design and analysis of a prototypic severe acute respiratory syndrome vaccine. *Chemical Biology and Drug Design*. 2009 Jan;73(1):53-61. PMCID: PMC2756483

c) Yang Y., Ringler P., Mueller S.A. and **Burkhard P**. Optimizing the refolding conditions of self-assembling polypeptide nanoparticles that serve as repetitive antigen display systems. *J Struct Biol.* 2012 Jan;177(1):168-176. PMID: 22115997

d) Indelicato G., Wahome N., Ringler P., Müller S.A., Nieh M., **Burkhard P** and Twarock R. Principles Governing the Self-Assembly of Coiled-Coil Protein Nanoparticles. *Biophys J*. 2016 Feb 2;110(3):646-660. PMCID: PMC4744166

4. Vaccine design using SAPNs

Using the SAPNs as a platform for vaccine design, I have demonstrated that the SAPNs can be used as a general platform for vaccine design. I have five different patents / patent applications dealing with the use of SAPNs for vaccine design (US8575110, US8546337, EP2766386A1, EP2766386A1, EP17157687.9). In the research labs of Alpha-O Peptides we have engineered five vaccine prototypes for four different infectious diseases that all are almost completely protective in animal challenge models. The clinical trials phase I/IIa of the most advanced vaccine (malaria) is currently planned to be finished next summer (2018). The five prototypes are: Malaria vaccine, HPV vaccine (L2-based), universal flu vaccine (M2e- and Helix C-based), seasonal flu vaccine (HA-based), toxoplasmosis vaccine. All of those prototypes are bacterially expressed, most of them are composed of one single protein chain. So, they can be produced very cheaply and rapidly. These five prototype vaccines show that the SAPN technology is indeed a platform technology that can be quickly adapted to pretty much any infectious disease (Ebola, Zika, Chikungunya, etc.). Furthermore, the SAPN technology can be used to engineer therapeutic vaccines for cancer, Alzheimer, addictions, obesity and many more.

a) Karch CP, Doll TAPF, Paulillo SM, Nebie I, Lanar DE, Corradin G, **Burkhard P** (2017). The Use of a P. falciparum Specific Coiled-coil Domain to Construct a Self-Assembling Protein Nanoparticle Vaccine to Prevent Malaria. *J. Nanobiotechnology*, 15 (1), 62 doi: 10.1186/s12951-017-0295-0

b) Kaba SA, Karch CP, Seth L, Ferlez KMB, Storme CK, Pesavento DM, Laughlin PY, Bergmann-Leitner ES, **Burkhard P**, Lanar DE (2018). Self-assembling protein nanoparticles with built-in flagellin domains increases protective efficacy of a Plasmodium falciparum based vaccine. *Vaccine* 36(6), 906-914. doi: 10.1016/j.vaccine.2017.12.001.

c) El-Bissati K, Zhou Y, Paulillo SM, Raman SK, Karch CP, Roberts CW, Lanar DE, Reed S, Fox C, Carter D, Alexander J, Sette A, Sidney J, Lorenzi H, Begeman IJ, **Burkhard P**, McLeod R (2017). Protein nanovaccine confers robust immunity against Toxoplasma. *Nature PJ Vaccines*, 2, doi:10.1038/s41541-017-0024-6.

d) Karch CP, Li J, Kulangara C, Paulillo SM, Raman SK, Emadi S, Tan A, Helal ZH, Fan Q, Khan MI, **Burkhard P**. Vaccination with self-adjuvanted protein nanoparticles provides protection against lethal influenza challenge. *Nanomedicine*. 2017 Jan;13(1):241-251. doi: 10.1016/j.nano.2016.08.030.

Complete List of Published Work in NCBI

https://www.ncbi.nlm.nih.gov/myncbi/collections/bibliography/42368162/

D. Research Support

Ongoing Research Support

None.

Completed Research Support

Development of novel IBV-nanoparticle based vaccine, its immunogenicity and protection studies in chickens

Role Co-PI Duration: 05/15 - 04/18 Funding agency: USDA-NIFA

Overall goal: To design protein nanoparticles as subunit vaccine against IBV.

Responsibilities: To direct the research in the Burkhard lab at UConn and coordinate with the research group of the PI M. Khan at the University of Connecticut.

GMP Production and Clinical Trial of a Self-Assembling Protein Nanoparticle and Toll-Like Receptor Liposomal MPL Adjuvanted Malaria Vaccine

Role Co-PI Duration: 07/15 - 06/17 Funding agency: CDRMP
Overall goal: To test a malaria vaccine based on self-assembling protein nanoparticles in clinical trials.
Responsibilities: To consult on the bio-production and vaccination protocols for the self-assembling protein nanoparticles developed at Alpha-O Peptides AG.

Malaria Vaccine Based on Self-Assembling Polypeptide Nanoparticles (SAPN)

Role PI Duration: 08/09 - 07/13 Funding agency: NIH-NIAID
Overall goal: This R01 proposal has the goal to design peptide nanoparticles as subunit vaccine against malaria.
Responsibilities: To direct the research at UConn and coordinate with the research group at WRAIR.

Atomic structure and assembly of Intermediate Filaments

Role PI Duration: 05/11 - 12/16 Funding agency: NIH-NIGMS
Overall goal: The goal of this PPG-project is to investigate the structural and biophysical properties of the intermediate filament protein vimentin
Responsibilities: To direct the research in the Burkhard lab at UConn and coordinate with the research group at Harvard, Northwestern and UPenn.

A peptide nanoparticle nicotine vaccine

Role PI Duration: 09/11 - 12/16 Funding agency: NIH-NIDA
Overall goal: This DP1 award aims at the development of a peptide nanoparticle nicotine vaccine and advance it through clinical trials phase I.
Responsibilities: To direct the whole project at UConn (protein design) at Alpha-O Peptides in Riehen (biophysical analysis), Switzerland and the Kantonsspital St. Gallen, Switzerland (clinical trials).

Peptide Nanoparticles as Novel Immunogens: Design and Analysis of Avian Influenza Vaccine

Role PI Duration: 12/11 - 11/16 Funding agency: USDA-NIFA
Overall goal: To design peptide nanoparticles as subunit vaccine against malaria.
Responsibilities: To direct the research in the Burkhard lab at UConn and coordinate with the research group of Dr. Khan (UConn - PI) and Gelb (University of Maryland).

OMB Number: 4040-0010
Expiration Date: 12/31/2022

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 1

ORGANIZATIONAL DUNS*: 046705849

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: The Regents of the University of California, Irvine

Start Date*: 09-01-2020 **End Date*:** 08-31-2021 **Budget Period: 1**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .		LBACHIR		BENMOHAMED		PD/PI	197,300.00	3			49,325.00	18,571.00	67,896.00
2 .		MICHAEL		BUCHMEIER		Co-Investigator	197,300.00	0.6			9,865.00	3,714.00	13,579.00
3 .		CHRISTINE		MCLAREN		Co-Investigator	194,815.00	0.6			9,741.00	3,667.00	13,408.00
4 .		ANTHONY		NESBURN		Co-Investigator	197,300.00	1			16,442.00	7,082.00	23,524.00
5 .		SEBASTIAN		SCHUBL		Co-Investigator	197,300.00	0.3			4,933.00	1,857.00	6,790.00
6 .		DONALD		FORTHAL		Co-Investigator	197,300.00	0.3			4,933.00	1,857.00	6,790.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **131,987.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
2	Post Doctoral Associates	24			125,105.00	29,921.00	155,026.00
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Data Analyst	1.2			8,637.00	4,449.00	13,086.00
3	**Total Number Other Personnel**					**Total Other Personnel**	**168,112.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**300,099.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PAR-20-178 . Received Date: 2020-05-22T18:02:25.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 1

ORGANIZATIONAL DUNS*: 046705849

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Irvine

Start Date*: 09-01-2020 **End Date*:** 08-31-2021 **Budget Period: 1**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,500.00
2. Foreign Travel Costs	
Total Travel Cost	**3,500.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 1

ORGANIZATIONAL DUNS*: 046705849

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Irvine

Start Date*: 09-01-2020 **End Date*:** 08-31-2021 **Budget Period: 1**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	36,500.00
2. Publication Costs	2,000.00
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	126,000.00
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8 . Animal Purchase & Husbandry	35,855.00
9 . Human Subjects Expenses	7,500.00
Total Other Direct Costs	**207,855.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**511,454.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Organized Research_On Campus	57	410,454.00	233,959.00
		Total Indirect Costs	**233,959.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number): DHHS, Helen Fung, (415) 437-7820

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**745,413.00**

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	745,413.00

L. Budget Justification* File Name: BudgetJustification_v81013861000.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0010
Expiration Date: 12/31/2022

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 2

ORGANIZATIONAL DUNS*: 046705849

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: The Regents of the University of California, Irvine

Start Date*: 09-01-2021 **End Date*:** 08-31-2022 **Budget Period: 2**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .		LBACHIR		BENMOHAMED		PD/PI	197,300.00	3			49,325.00	19,023.00	68,348.00
2 .		MICHAEL		BUCHMEIER		Co-Investigator	197,300.00	0.6			9,865.00	3,805.00	13,670.00
3 .		CHRISTINE		MCLAREN		Co-Investigator	197,300.00	0.6			9,865.00	3,805.00	13,670.00
4 .		ANTHONY		NESBURN		Co-Investigator	197,300.00	1			16,442.00	7,263.00	23,705.00
5 .		SEBASTIAN		SCHUBL		Co-Investigator	197,300.00	0.3			4,933.00	1,902.00	6,835.00
6 .		DONALD		FORTHAL		Co-Investigator	197,300.00	0.3			4,933.00	1,902.00	6,835.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **133,063.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
2	Post Doctoral Associates	24			128,857.00	31,720.00	160,577.00
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Data Analyst	1.2			8,896.00	4,700.00	13,596.00
3	**Total Number Other Personnel**					**Total Other Personnel**	**174,173.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**307,236.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PAR-20-178 . Received Date: 2020-05-22T18:02:25.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 2

ORGANIZATIONAL DUNS*: 046705849

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Irvine

Start Date*: 09-01-2021 **End Date*:** 08-31-2022 **Budget Period: 2**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,605.00
2. Foreign Travel Costs	
Total Travel Cost	**3,605.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 2

ORGANIZATIONAL DUNS*: 046705849

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Irvine

Start Date*: 09-01-2021 **End Date*:** 08-31-2022 **Budget Period: 2**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	37,595.00
2. Publication Costs	2,060.00
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	126,000.00
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8 . Animal Purchase & Husbandry	27,458.00
9 . Human Subjects Expenses	7,500.00
Total Other Direct Costs	**200,613.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**511,454.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Organized Research_On Campus	57	385,454.00	219,709.00
		Total Indirect Costs	**219,709.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number): DHHS, Helen Fung, (415) 437-7820

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**731,163.00**

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	731,163.00

L. Budget Justification* File Name: BudgetJustification_v81013861000.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0010
Expiration Date: 12/31/2022

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 3

ORGANIZATIONAL DUNS*: 046705849

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: The Regents of the University of California, Irvine

Start Date*: 09-01-2022 **End Date*:** 08-31-2023 **Budget Period: 3**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .		LBACHIR		BENMOHAMED		PD/PI	197,300.00	6			98,650.00	39,016.00	137,666.00
2 .		MICHAEL		BUCHMEIER		Co-Investigator	197,300.00	0.6			9,865.00	3,902.00	13,767.00
3 .		CHRISTINE		MCLAREN		Co-Investigator	197,300.00	0.6			9,865.00	3,902.00	13,767.00
4 .		ANTHONY		NESBURN		Co-Investigator	197,300.00	1			16,442.00	7,444.00	23,886.00
5 .		SEBASTIAN		SCHUBL		Co-Investigator	197,300.00	0.3			4,933.00	1,951.00	6,884.00
6 .		DONALD		FORTHAL		Co-Investigator	197,300.00	0.3			4,933.00	1,951.00	6,884.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **202,854.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
2	Post Doctoral Associates	24			132,723.00	33,623.00	166,346.00
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Data Analyst	1.2			9,163.00	4,969.00	14,132.00
3	**Total Number Other Personnel**					**Total Other Personnel**	**180,478.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**383,332.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PAR-20-178 . Received Date: 2020-05-22T18:02:25.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 3

ORGANIZATIONAL DUNS*: 046705849

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Irvine

Start Date*: 09-01-2022 **End Date*:** 08-31-2023 **Budget Period: 3**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,713.00
2. Foreign Travel Costs	
Total Travel Cost	**3,713.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 3

ORGANIZATIONAL DUNS*: 046705849

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Irvine

Start Date*: 09-01-2022 **End Date*:** 08-31-2023 **Budget Period: 3**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	38,723.00
2. Publication Costs	2,122.00
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8 . Animal Purchase & Husbandry	72,109.00
Total Other Direct Costs	**112,954.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**499,999.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Organized Research_On Campus	57	499,999.00	284,999.00
		Total Indirect Costs	**284,999.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number): DHHS, Helen Fung, (415) 437-7820

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**784,998.00**

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	784,998.00

L. Budget Justification*	File Name: BudgetJustification_v81013861000.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 4

ORGANIZATIONAL DUNS*: 046705849

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: The Regents of the University of California, Irvine

Start Date*: 09-01-2023 **End Date*:** 08-31-2024 **Budget Period: 4**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .		LBACHIR		BENMOHAMED		PD/PI	197,300.00	6			98,650.00	39,920.00	138,570.00
2 .		MICHAEL		BUCHMEIER		Co-Investigator	197,300.00	0.6			9,865.00	3,992.00	13,857.00
3 .		CHRISTINE		MCLAREN		Co-Investigator	197,300.00	0.6			9,865.00	3,992.00	13,857.00
4 .		ANTHONY		NESBURN		Co-Investigator	197,300.00	1			16,442.00	7,628.00	24,070.00
5 .		SEBASTIAN		SCHUBL		Co-Investigator	197,300.00	0.3			4,933.00	1,996.00	6,929.00
6 .		DONALD		FORTHAL		Co-Investigator	197,300.00	0.3			4,933.00	1,996.00	6,929.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **204,212.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
2	Post Doctoral Associates	24			136,705.00	35,725.00	172,430.00
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Data Analyst	1.2			9,438.00	5,252.00	14,690.00
3	**Total Number Other Personnel**					**Total Other Personnel**	**187,120.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**391,332.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 4

ORGANIZATIONAL DUNS*: 046705849

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Irvine

Start Date*: 09-01-2023 **End Date*:** 08-31-2024 **Budget Period: 4**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,825.00
2. Foreign Travel Costs	
Total Travel Cost	**3,825.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 4

ORGANIZATIONAL DUNS*: 046705849

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Irvine

Start Date*: 09-01-2023 **End Date*:** 08-31-2024 **Budget Period: 4**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	39,885.00
2. Publication Costs	2,185.00
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8 . Animal Purchase & Husbandry	62,772.00
Total Other Direct Costs	**104,842.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**499,999.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Organized Research_On Campus	57	499,999.00	284,999.00
		Total Indirect Costs	**284,999.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number): DHHS, Helen Fung, (415) 437-7820

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**784,998.00**

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	784,998.00

L. Budget Justification*	File Name: BudgetJustification_v81013861000.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

Tracking Number: GRANT13114391 Funding Opportunity Number: PAR-20-178 . Received Date: 2020-05-22T18:02:25.000-04:00

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 5

ORGANIZATIONAL DUNS*: 046705849

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: The Regents of the University of California, Irvine

Start Date*: 09-01-2024 **End Date*:** 08-31-2025 **Budget Period: 5**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .		LBACHIR		BENMOHAMED		PD/PI	197,300.00	6			98,650.00	40,742.00	139,392.00
2 .		MICHAEL		BUCHMEIER		Co-Investigator	197,300.00	0.6			9,865.00	4,074.00	13,939.00
3 .		CHRISTINE		MCLAREN		Co-Investigator	197,300.00	0.6			9,865.00	4,074.00	13,939.00
4 .		ANTHONY		NESBURN		Co-Investigator	197,300.00	1			16,442.00	7,792.00	24,234.00
5 .		SEBASTIAN		SCHUBL		Co-Investigator	197,300.00	0.3			4,933.00	2,037.00	6,970.00
6 .		DONALD		FORTHAL		Co-Investigator	197,300.00	0.3			4,933.00	2,037.00	6,970.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **205,444.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
2	Post Doctoral Associates	24			140,805.00	37,736.00	178,541.00
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Data Analyst	1.2			9,721.00	5,531.00	15,252.00
3	**Total Number Other Personnel**					**Total Other Personnel**	**193,793.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**399,237.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 5

ORGANIZATIONAL DUNS*: 046705849

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Irvine

Start Date*: 09-01-2024 **End Date*:** 08-31-2025 **Budget Period: 5**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,939.00
2. Foreign Travel Costs	
Total Travel Cost	**3,939.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 5

ORGANIZATIONAL DUNS*: 046705849

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Irvine

Start Date*: 09-01-2024 **End Date*:** 08-31-2025 **Budget Period: 5**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	41,081.00
2. Publication Costs	2,251.00
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8 . Animal Purchase & Husbandry	53,491.00
Total Other Direct Costs	**96,823.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**499,999.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Organized Research_On Campus	57	499,999.00	284,999.00
		Total Indirect Costs	**284,999.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number): DHHS, Helen Fung, (415) 437-7820

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**784,998.00**

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	784,998.00

L. Budget Justification*	File Name: BudgetJustification_v81013861000.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

Tracking Number: GRANT13114391 Funding Opportunity Number: PAR-20-178 . Received Date: 2020-05-22T18:02:25.000-04:00

BUDGET JUSTIFICATION

KEY PERSONNEL:

Lbachir BenMohamed, Ph. D. Principal Investigator **3.0 CM for Yr 1-2, & 6.0 CM for Yr 3-5**
Dr. BenMohamed (Professor/Director of Cellular and Molecular Immunology Laboratory) is is a faculty member at the Gavin Herbert Eye Institute and has joint appointments at the Institute for Immunology of the University of California Irvine (UCI).

Dr. BenMohamed is an immunologist and virologist that graduated from Pasteur Institute, Paris, France, with a strong career focus on vaccine development against infectious viral pathogens, including Coronaviruses. I will bring to the project more than 30 years of experience in cellular and molecular immune responses to infectious pathogens. He has authored more than 100 peer-reviewed papers on immunology, virology and vaccine development.

He is a leading researcher in viral vaccines and immunotherapy. For the last 20 years, the Dr. BenMohamed has accumulated extensive research experience in the field of immunity and immunopathology and vaccine development against many viral pathogens from The Pasteur Institute (Paris), The City of Hope National Medical Center, Cedars Sinai Medical Center and more recently in the Laboratory of Cellular and Molecular Immunology at UCI. Dr. BenMohamed will be directly involved in immunization and studying the immunogenicity and protective efficacy of SAPN-based for vaccine against coronavirus SARS-CoV2 in "humanized" susceptible 6255 model. He will also provide expert guidance regarding the construction of SARS-CoV2 proteins-SAPN to the Co-Investigator and he will supervise a post-doctoral that will be involved in the mouse experiments (see below).

Michael J. Buchmeier, Ph. D. **Co-Investigator** **0.6 Calendar Months**
We are requesting 0.60 calendar month time and effort for this highly regarded Coronavirus expect and virologist at UC Irvine, and a long-term collaborator of Dr. BenMohamed. The PI and Co-PI have an established collaboration for the last 4 years investigating the Coronavirus immune evasion mechanisms, inflammation and immune correlates of protection during herpes latency. They have successfully co-authored many publications including the exhaustion of virus-specific $CD8^+$ T cells as described in this proposal.

Donald Forthal, MD. **Co-Investigator** **0.3 Calendar Months**
Dr. Forthal, an infectious disease specialist and virus immunopathology expert who currently seen COVID-19 patient at UC Irvine Medical center. Dr. Forthal will devote effort as needed will help recruit symptomatic and asymptomatic COVID-19 patients and clinical analyzing of their symptoms. He will also be involved in delivering blood and saliva from symptomatic and asymptomatic COVID-19 patients together with Dr. Schubl .

Sebastian Dominik Schubl, MD, FACS. **Co-Investigator** **0.3 Calendar Months**
Dr. Schubl, a pulmonary specialist and lung inflammation expert who currently treat COVID-19 patient at UC Irvine Medical center. Dr. Schubl will devote effort as needed will help recruit symptomatic and asymptomatic COVID-19 patients and clinical analyzing of their symptoms. He will also be involved in delivering blood and saliva from symptomatic and asymptomatic COVID-19 patients.

Anthony Nesburn, M. D. **Co-Investigator** **1.0 Calendar Months**
For the clinical aspects of this proposal there is Dr. Nesburn, a world leader and expert in clinical infectious diseases. He devote effort as needed to help recruit symptomatic and asymptomatic patients and help analyze the clinical aspect of COVID-19 disease. Dr. Nesburn will also help corelate the clinical severity and symptoms of COVID-19 with the immunological results produced in dr. Benmohamed. Dr. BenMohamed and Dr. Nesburn laboratories are located side by side facilitating daily interaction.

Christine McLaren, Ph. D. **Co-Investigator** **0.6 Calendar Months**
We are requesting 0.6 calendar month time and effort for Dr. McLaren, the Director of Biostatistics at the Department of Epidemiology (UC, Irvine). Dr. McLaren is a professor of Epidemiology and Bio-statistics at UC Irvine and will help with the statistical analysis as described in this application. Dr. BenMohamed and Dr. McLaren have been collaborating for the last 6 years on many ongoing herpes immunology projects. Dr.

McLaren will help analyze the statistics of the *in vitro*, *in situ, ex vivo*, and *in vivo* results. She will also analyze the statistics comparing the contribution of the peripheral epithelial T cell immunity (at the VMC) epithelium vs. central neuronal T cell immunity (at the DRG) in protection against recurrent genital herpes. This will include: (**1**) Statistical analysis to capture the $CD4^+$ and $CD8^+$ T_{RM} cell dynamics of the containment within SARS-COV-2 infected DRG and VMC. This includes statistical analysis of SARS-COV-2 reactivation from DRG based on observed patterns of single neuron loads and $CD4^+$ and $CD8^+$ T cell infiltration and SARS-COV-2 shedding rate from VMC; and (**2**) Statistical analysis to characterize the duration of protection, and the protective mechanisms induced by the prime/pull vaccine in the mice model. In doing so, we expect the statistical analysis, to help determine relative contribution of the peripheral epithelial T cell immunity epithelium vs. central neuronal T cell immunity in protection against recurrent genital herpes.

NON-KEY PERSONNEL

Ruchi Srivastava Ph. D. **Post-doctoral fellow** **12 Calendar Months**

We are requesting 12 calendar month time and effort for the Post-doctoral fellow, Dr. Srivastava has been working on in cellular and molecular immunology and inflammation projects in Dr. BenMohamed laboratory for past 5 year. Her principal task will be to carry out in vitro and in vivo immunological experiments described in this application. Specifically, she will be responsible for synthetic peptide handling and storage, cell culture, flow cytometry assay, Luminex assay, cell sorting, generation of antigen presenting cells, T-cell functional assays, RNASeq assay, pro- and anti-inflammatory cytokine Luminex and ELISPOT assays, FACS and confocal microscopy as described in this project. She will study the $CD4^+$ and $CD8^+$ T cell responses to SAPN vaccine candidates in [redacted] model COVID-19. She will assist the PI with the large amount of [redacted] required for analysis immunogenicity and protective efficacy described in this application. Dr. BenMohamed will supervise this postdoctoral fellow. They will meet weekly to discuss results of vaccine evaluation. Dr. Dhanushkodi will also be responsible for maintaining [redacted] and ordering supplies.

To Be Named **Post-doctoral fellow** **12 Calendar Months**

We are requesting 12 calendar month time and effort for a Graduate student in the Molecular Immunology, Virology and inflammation training program. As part of his/her dissertation research under Dr. BenMohamed' mentorship he/she will perform all studies [redacted]

Angele Nalbandian Ph. D. **Data Analyst** **1.2 Calendar Months**

We are requesting 1.2 calendar month time for Angele Nalbandian to provide data analysis for the project. She will be involved in analyzing the single cell scRNASeq data of $CD4^+$ and $CD8^+$ T cells from mices that were immunized with each of the 19 vaccine candidates as well as controls.

James V. Jester, Ph. D. **Other Significant Contributor** **<0.1 Calendar Months**

Dr. Jester will devote effort as needed on confocal microscopy and imaging expert. Dr. Jester whose lab is adjacent to principal investigator lab will help confocal microscopy aspect of this proposal, including lungs and brain tissues screening by microscopy. He is an imaging specialist at UC Irvine. He will be available on an as needed basis to help with performing and analyzing the confocal microscopy experiments. This includes confocal microscopy three-dimensionally at high-resolution on a macroscopic scale of $CD4^+$ and $CD8^+$ T cell infiltrates into lungs and brain tissues lesions; and three-dimensionally at high-resolution on a macroscopic scale of $CD4^+$ and $CD8^+$ T cell infiltrates surrounding infected epithelial cells, fibroblasts/keratinocytes and neuronal axons in lungs and brain tissues and $CD4^+$ and $CD8^+$ T cell infiltrates surrounding neuronal body in the brain of vaccinated and control mice.

Eric Pearlman, Ph. D. **Other Significant Contributor** **<0.1 Calendar Months**

Dr. Pearlman, a specialist in inflammation will devote effort as needed will help analyze the inflammation and cytokine storm. He will also be involved in delivering AAV8 vectors expressing T-cell attracting chemokines.

Lanny Hsieh, M.D. **Other Significant Contributor** **<0.1 Calendar Months**
Dr. Hsieh, is Health Sciences Clinical Professor a specialist in infectious disease and the Medical Direcotr for the Clinical Documentation Improvement project. She will devote effort as needed to help recruit symptomatic and asymptomatic patients and help analyze the clinical aspect of COVID-19 disease.

"Salaries for all personnel are based upon current University of California academic and staff salary scales. All personnel budget calculations include salary range adjustments (3%) as applicable for each year of support in accordance with published University guidelines. Fringe benefit rates for personnel were derived using composite benefit rates agreed upon by the University of California Office of the President and the DHHS Audit Agency, the Cognizant Audit Agency for the University of California. http://research.uci.edu/sponsored-projects/rates-fees/fringe-benefits.html. Vacation leave accruals are excluded from the composite benefit rate and are assessed at 7%."

MATERIALS AND SUPPLIES:

Lab Consumables, Cell Culture, Reagents, disposable plastic, antibodies ($193,783): We are requesting a total budget of $36,500 for year 1 with sub sequential increase of 3% for the following project years duration for lab consumables, cell culture reagents. This includes bottles of tissue culture medium to support our in vitro measurements of T cell responses to our various vaccine constructs, as well as gloves, test kits including mycoplasma and endotoxin, safety supplies, gowns, sterile syringes and needles, and other miscellaneous supplies necessary for a routine functional laboratory. We are also asking for a yearly budget for the purchase of all of the required plastic ware that is normally used in the laboratory for in vitro maintenance of cell cultures, measurement of T cell responses, and molecular biology and virology applications. This includes flasks of all sizes, plates between 6 and 96 wells for virus harvesting, disposable pipettes between 1 and 25 ml volume, purification flasks, barrier tips, and other necessary plastics to carry out the experiments described in the proposal. This category will include other disposable items such as cell scrapers, troughs, Eppendorf multi-channel tips, and all other liquid handling supplies. The proposed studies will utilize a variety of fluorescently conjugated antibodies (approximately $8,000/year), real time PCR reagents for quantifying viral genomes, kits for genotyping mice, viscoelastic antibiotics, anesthesia (approximately $540.00/year), reagents for magnetic sorting of cells, and extensive use of disposable plastic ware for performing in vitro immunologic assays, maintaining cell lines, performing injections, etc. (approximately $20,500/year). Use of Flow Cytometry: 16hrs/month @ $50/hr (approximately $7450/Year). Based on preliminary work we estimate the cost of these reagents and supplies to be approximately $38,757 each year over the five-year grant period.

OTHER DIRECT COST:

Publication Costs ($10,618): Funds for publication-related expenses are requested in all years to cover the cost of manuscript fees, purchasing reprints, color figures, and poster costs associated with the dissemination of research results at national scientific conferences. These costs were estimated using the published reprint and page charges based on historical costs. An approximately $2,124 each year to defray cost related to publication of two manuscripts yearly, which is the average per grant for the last 5 years of our laboratory productivity.

[redacted] **($251,685):** [redacted]

[redacted]

6255

[redacted]

Human Subjects Expense ($15,000): 150 patients x $50 per patient for years 1 and 2.
Human Subjects compensation related to blood draw (daily parking fee + study participation payment).

Sub-awards/Consortium/Contractual Costs ($252,000): Sunomix therapeutics will be responsible to deliver the proteins-based SAPNs to Dr. Lbachir BenMohamed Lab at UCI, California, to be used for the Herpes vaccine grant. As Sunomix Therapeutics, Dr. Burkhard and Dr. Bouziane will be directly involved in the design, development, cloning, protein expression, purification, refolding, TLR-activation and analysis of SAPN prototype to make them suitable as a platform for SARS-COV vaccine. At least ten COVID proteins-based SAPNs identified from herpes genome in Dr. BenMohamed lab will be produced at Sunomix Therapeutics. All the nanoparticles will contain CpG, the preliminary data using SAPNs produced by Sunomix Therapeutics shows very promising results.

FACILITIES AND ADMINISTRATIVE EXPENSES

F&A costs were estimated in accordance with UCI's rate agreement approved by the Department of Health and Human Services, the Federal Cognizant Audit Agency on 5/29/2019. UCI's period of agreement covers a five-year period beginning July 1, 2016 and ending June 30, 2021. The established on-campus research rates are set at:

- 56% for the period 7/1/2019 – 6/30/2020
- 57% for the period 7/1/2020 and beyond

Organized research F&A cost rates are applied to the Modified Total Direct Costs (MTDC) base on a pro rata basis when project start dates are other than July 1. The MTDC base is the total direct costs for a project less those budget items that are excluded by agreement with the audit agency. The excluded costs are: equipment, construction, alterations and renovations, hospital or clinic charges for patient care, space rental or lease, tuition and fee remission, scholarships, and the amount that exceeds $25,000 of any subaward.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals ($)	
Section A, Senior/Key Person		877,560.00
Section B, Other Personnel		903,676.00
Total Number Other Personnel	15	
Total Salary, Wages and Fringe Benefits (A+B)		1,781,236.00
Section C, Equipment		
Section D, Travel		18,582.00
1. Domestic	18,582.00	
2. Foreign		
Section E, Participant/Trainee Support Costs		
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other		
6. Number of Participants/Trainees		
Section F, Other Direct Costs		723,087.00
1. Materials and Supplies	193,784.00	
2. Publication Costs	10,618.00	
3. Consultant Services		
4. ADP/Computer Services		
5. Subawards/Consortium/Contractual Costs	252,000.00	
6. Equipment or Facility Rental/User Fees		
7. Alterations and Renovations		
8. Other 1	251,685.00	
9. Other 2	15,000.00	
10. Other 3		
Section G, Direct Costs (A thru F)		2,522,905.00
Section H, Indirect Costs		1,308,665.00
Section I, Total Direct and Indirect Costs (G + H)		3,831,570.00
Section J, Fee		
Section K, Total Costs and Fee (I + J)		3,831,570.00

OMB Number: 4040-0010
Expiration Date: 12/31/2022

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 1

ORGANIZATIONAL DUNS*: 080437688

Budget Type*: ❍ Project ● Subaward/Consortium

Enter name of Organization: Sunomix Therapeutics

Start Date*: 09-01-2020 **End Date*:** 08-31-2021 **Budget Period: 1**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .		Peter		Burkhard		Other	0.00	0.01			0.00	0.00	0.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **0.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
2	Project Scientists	11			90,445.00	0.00	90,445.00
2	**Total Number Other Personnel**					**Total Other Personnel**	**90,445.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**90,445.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Tracking Number: GRANT13114391 Funding Opportunity Number: PAR-20-178 . Received Date: 2020-05-22T18:02:25.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 1

ORGANIZATIONAL DUNS*: 080437688

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: Sunomix Therapeutics

Start Date*: 09-01-2020 **End Date*:** 08-31-2021 **Budget Period: 1**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 1

ORGANIZATIONAL DUNS*: 080437688
Budget Type*: ❍ Project ● Subaward/Consortium
Organization: Sunomix Therapeutics

Start Date*: 09-01-2020 **End Date*:** 08-31-2021 **Budget Period: 1**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	24,100.00
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	**24,100.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**114,545.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Subrecipient_Indirect_Cost_Rate	10	114,545.00	11,455.00
		Total Indirect Costs	**11,455.00**

Cognizant Federal Agency
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**126,000.00**

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	126,000.00

L. Budget Justification*	File Name: Budget_Just_R01_Sunomix_UCI_v21013784429.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 2

ORGANIZATIONAL DUNS*: 080437688

Budget Type*: ❍ Project ● Subaward/Consortium

Enter name of Organization: Sunomix Therapeutics

Start Date*: 09-01-2021 **End Date*:** 08-31-2022 **Budget Period: 2**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .		Peter		Burkhard		Other	0.00	0.01			0.00	0.00	0.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **0.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
2	Project Scientist	11			90,445.00	0.00	90,445.00
2	**Total Number Other Personnel**					**Total Other Personnel**	**90,445.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**90,445.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 2

ORGANIZATIONAL DUNS*: 080437688

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: Sunomix Therapeutics

Start Date*: 09-01-2021 **End Date*:** 08-31-2022 **Budget Period: 2**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 2

ORGANIZATIONAL DUNS*: 080437688
Budget Type*: ❍ Project ● Subaward/Consortium
Organization: Sunomix Therapeutics

Start Date*: 09-01-2021 **End Date*:** 08-31-2022 **Budget Period: 2**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	24,100.00
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	**24,100.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**114,545.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Subrecipient_Indirect_Cost_Rate	10	114,545.00	11,455.00
		Total Indirect Costs	**11,455.00**

Cognizant Federal Agency
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**126,000.00**

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	126,000.00

L. Budget Justification*	File Name: Budget_Just_R01_Sunomix_UCI_v21013784429.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0010
Expiration Date: 12/31/2022

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 3

ORGANIZATIONAL DUNS*: 080437688

Budget Type*: ❍ Project ● Subaward/Consortium

Enter name of Organization: Sunomix Therapeutics

Start Date*: 09-01-2022 **End Date*:** 08-31-2023 **Budget Period: 3**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .		Peter		Burkhard		Other	0.00	0.01			0.00	0.00	0.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **0.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Total Number Other Personnel					**Total Other Personnel**	
					Total Salary, Wages and Fringe Benefits (A+B)		**0.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PAR-20-178 . Received Date: 2020-05-22T18:02:25.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 3

ORGANIZATIONAL DUNS*: 080437688

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: Sunomix Therapeutics

Start Date*: 09-01-2022 **End Date*:** 08-31-2023 **Budget Period: 3**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 3

ORGANIZATIONAL DUNS*: 080437688
Budget Type*: ❍ Project ● Subaward/Consortium
Organization: Sunomix Therapeutics

Start Date*: 09-01-2022 **End Date*:** 08-31-2023 **Budget Period: 3**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	**0.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**0.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Subrecipient_Indirect_Cost_Rate	10	0.00	0.00
		Total Indirect Costs	**0.00**

Cognizant Federal Agency
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**0.00**

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	0.00

L. Budget Justification*	File Name: Budget_Just_R01_Sunomix_UCI_v21013784429.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 4

ORGANIZATIONAL DUNS*: 080437688

Budget Type*: ❍ Project ● Subaward/Consortium

Enter name of Organization: Sunomix Therapeutics

Start Date*: 09-01-2023 **End Date*:** 08-31-2024 **Budget Period: 4**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .		Peter		Burkhard		Other	0.00	0.01			0.00	0.00	0.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **0.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Total Number Other Personnel					**Total Other Personnel**	
					Total Salary, Wages and Fringe Benefits (A+B)		**0.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 4

ORGANIZATIONAL DUNS*: 080437688

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: Sunomix Therapeutics

Start Date*: 09-01-2023 **End Date*:** 08-31-2024 **Budget Period: 4**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 4

ORGANIZATIONAL DUNS*: 080437688
Budget Type*: ❍ Project ● Subaward/Consortium
Organization: Sunomix Therapeutics

Start Date*: 09-01-2023 **End Date*:** 08-31-2024 **Budget Period: 4**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	**0.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**0.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Subrecipient_Indirect_Cost_Rate	10	0.00	0.00
		Total Indirect Costs	**0.00**

Cognizant Federal Agency
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**0.00**

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	0.00

L. Budget Justification*	File Name: Budget_Just_R01_Sunomix_UCI_v21013784429.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0010
Expiration Date: 12/31/2022

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 5

ORGANIZATIONAL DUNS*: 080437688

Budget Type*: ❍ Project ● Subaward/Consortium

Enter name of Organization: Sunomix Therapeutics

Start Date*: 09-01-2024 **End Date*:** 08-31-2025 **Budget Period: 5**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .		Peter		Burkhard		Other	0.00	0.01			0.00	0.00	0.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **0.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Total Number Other Personnel					**Total Other Personnel**	
					Total Salary, Wages and Fringe Benefits (A+B)		**0.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PAR-20-178 . Received Date: 2020-05-22T18:02:25.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 5

ORGANIZATIONAL DUNS*: 080437688

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: Sunomix Therapeutics

Start Date*: 09-01-2024 **End Date*:** 08-31-2025 **Budget Period: 5**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 5

ORGANIZATIONAL DUNS*: 080437688
Budget Type*: ❍ Project ● Subaward/Consortium
Organization: Sunomix Therapeutics

Start Date*: 09-01-2024 **End Date*:** 08-31-2025 **Budget Period: 5**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	**0.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**0.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Subrecipient_Indirect_Cost_Rate	10	0.00	0.00
		Total Indirect Costs	**0.00**

Cognizant Federal Agency
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**0.00**

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	0.00

L. Budget Justification*	File Name: Budget_Just_R01_Sunomix_UCI_v21013784429.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

BUDGET JUSTIFICATION Sunomix Therapeutics, San Diego, CA
UCI Grant R01 Titled: Developing a Multi-epitope Pan-Coronavirus Vaccine
UCI PI: Dr Lbachir Benmohamed

Year 1: $114,545.00 Direct Cost + $11,455.00 Indirect Cost (10%) Total Cost $126,000.00
Year 2: $114,545.00 Direct Cost + $11,455.00 Indirect Cost (10%) Total Cost $126,000.00

We are requesting a total cost budget over 2 years duration of $ 252,000.00

Year 1: $114,545.00 Direct Cost + $11,455.00 Indirect Cost (10%) Total Cost $126,000.00

PERSONNEL:

Peter Burkhard, Ph. D. Consortium PI <0.1 Calendar Months

Dr. Burkhard, a specialist in SAPNs nanoparticles will devote effort as needed will help design and produce SAPN-based vaccines as described in this proposal.

Mohammed Bouziane, Ph. D Consortium Scientist 2.0 Calendar Months $35,000

Dr. Bouziane have extensive experience in leading multi-disciplinary groups from Discovery, R&D to preclinical, and early clinical programs. Strong and broad scientific expertise covering multiple areas of genomics, proteomics, mutagenesis, nanoparticles SAPNs, diagnostics, vaccines and cell therapies for the treatment of infectious diseases, cancer and immunotherapies.

I am the Collaborator on this this Covid 19 SAPN vaccine project and I am responsible for its conception and in coordinating the collaboration.
Sunomix Therapeutics will be responsible to deliver the SAPNs to Dr. Lbachir Benmohamed Lab at UCI, California, to be used for the COVID 19 vaccine grant.

As Sunomix Therapeutics CEO, Dr. Bouziane will be directly involved in the design, development, cloning, protein expression, purification, refolding, TLR-activation and analysis of SAPN prototype to make them suitable as a platform for COVID 19 vaccine. At least ten prototype that contain different pairs of CD4 and CD8 human epitopes identified from COVID genome in Dr. Benmohamed lab will be produced at Sunomix Therapeutics. All the nanoparticles will contain CpG, the preliminary data using SAPNs produced by Sunomix Therapeutics shows very promising results. Dr. Bouziane will also assist the PI with the in vivo work and data analysis as described in this application. He will supervise a postdoctoral fellow. They will meet weekly to discuss results of SAPNs bio production.

To Be Named Post doc-Sr. Scientist 9.0 Calendar Months $55,445

We are requesting 9.0 calendar months time and effort for this postdoctoral fellow. He will be responsible for the bio production of SAPNs under Dr. Bouziane supervision including: construction design, PCR, cloning, sequencing, protein expression, purification, refolding, TLR-activation and analysis of SAPN prototype to make them suitable as a platform for HSV vaccine. At least ten prototype that contain different pairs of CD4 and CD8 human epitopes identified from herpes genome in Dr. BenMohamed will be produced. He will also assist the CO-PI data analysis and working with Alpha-O-peptides.

MATERIALS AND SUPPLIES:

Lab Consumables, Molecular Biology, Gene synthesis-Cloning, Sequencing of 5 Covid19 SAPNs.
We are requesting a total budget over 1 year duration of: $ 8,500
The DNA coding for the 5 nanoparticles SAPNs constructs will be prepared using standard molecular biology procedures. Plasmids containing the DNA coding for the protein sequence are constructed by cloning into the suitable (mostly NcoI, BamHI, NheI and EcoRI) restriction sites of the basic SAPN expression plasmid. This construct is composed of a pentameric coiled-coil tryptophane zipper linked by a glycine residues to a trimeric de-novo designed leucine coiled coil that for some constructs contains a panDR binding CD4+ epitope string. At the C-terminus the protein chain may be extended by a flagellin construct composed of the D0 and D1 domains of Salmonella enterica flagellin from the structure with pdb-code 3V47 from the RCSB protein data bank as in the prototype.
We need molecular biology Kits and reagents for PCR, cloning, lab consumables to support our in vitro experiments for our various vaccine constructs, as well as gloves, test kits including mycoplasma and endotoxin, safety supplies and other miscellaneous supplies necessary for a routine functional laboratory.
We are also asking for a yearly budget for the purchase of all of the required plastic ware that is normally used in the laboratory for PCR and molecular biology and virology applications. This includes flasks of all sizes, plates between 6 and 96 wells for PCR, disposable pipettes between 1 and 25 ml volume, barrier tips, and other necessary plastics to carry out the experiments described in the proposal. This category will include other disposable items such as Eppendorf multi-channel tips, and all other liquid handling supplies.

Lab Consumables, Protein Expression, Large scale production of 5 Covid19 SAPNs:
We are requesting a total budget over 1 year duration of: $6,000
The plasmids for 5 SAPNs are transformed into Escherichia coli BL21 (DE3) cells. Expression is induced with isopropyl β-D-thiogalacto-pyranoside. Alternatively, also other cell lines can be used for expression, such as tuner or KRX cells. Diluting the pre-cultures into the expression culture. The protein expression level is assessed polyacrylamide gel electrophoresis (SDS-PAGE).
We need bottles of tissue culture medium for scale up production of various vaccine constructs, as well as gloves, SDS-PAGE, test kits, safety supplies, gowns, sterile syringes and needles, and other miscellaneous supplies necessary for a routine functional laboratory. We are also asking for a yearly budget for the purchase of all of the required plastic ware that is normally used in the laboratory for in vitro maintenance of cell cultures and protein expression. This includes flasks of all sizes, disposable pipettes between 1 and 25 ml volume, purification flasks, barrier tips, and other necessary plastics to carry out the experiments described in the proposal. This category will include other disposable items such as Eppendorf multi-channel tips, and all other liquid handling supplies.

Lab Consumables, Protein Purification, Refolding of 5 Covid19 SAPNs:
We are requesting a total budget over 1 year duration of: $9,600
Protein purification for **5 Covid19** SAPNs constructs.
We are also asking for a yearly budget for the purchase of all of the required protein purification and sequencing including:
Ni-NTA Agarose Beads (Qiagen, Valencia, CA, USA)
Purification columns
Lysis, elution buffers
SDS-PAGE.
Protein refolding. For refolding the protein is first rebuffered in specific buffer solution without urea. This quick dilution from denaturing (urea) to native (no urea) buffer conditions triggers refolding of the

protein. The solution is then analyzed by negative stain transmission electron microscopy at different resolutions. If needed further screens for optimal refolding conditions can be performed with smaller sampling sizes of the pH and the ionic strength. Additionally, excipients such as trehalose, sucrose, arginine, proline or others can be added, or if needed detergents such as cholate, deoxycholate, tween-80 or others can be added.

TLR-activation. Activation through TLR5 will be assessed for different SAPN prototypes. The testing will be done using TLR/NF-kB/ SEAPorter™ Stably Transfected HEK 293 Stable Cell Lines as follows: All cell lines are stably co-transfected cell lines, which expresses the TLR5 and the secreted alkaline phosphatase (SEAP) reporter gene under the transcriptional control of an NF-kB response element. Using the 96-well plate format assays, TLR/NF-kB/SEAPorter™ HEK 293 cell line are used for screening of compounds as potential TLR5 agonists. The extent of SEAP secreted into the media is indicative of the amount of agonist activity. SEAP catalyzes the hydrolysis of p-Nitrophenyl phosphate (PNPP) producing a yellow product that can be read in a spectrophotometer or ELISA reader at 405 nm. Different concentrations of compounds are used to yield an EC50 value for each compound tested. Positive controls are made using native flagellin. Each compound will be tested in duplicate. Standard methodology for agonist testing is incubation of compounds in triplicate in 96 well plates at 5X104 cells/well.

Cells are stimulated with control ligand or test compounds at various concentrations. After 24 hour incubation SEAP is analyzed using SEAPorter™ Assay Kit. Dose-responsive percent activation of each sample well will be calculated to yield the ligand EC50 value.

Analysis of the biophysical properties of the SAPNs. The shape and size of the SAPNs will be analyzed using Transmission Electron Microscopy (TEM) and Dynamic Light Scattering (DLS).

Total Direct Cost $114,545.00

Total In direct Cost Fringe benefit (10%) $11,455.00

Year 2: $114,545.00 Direct Cost + $11,455.00 Indirect Cost (10%) Total Cost $126,000.00
PERSONNEL:

Peter Burkhard, Ph. D. Consortium PI <0.1 Calendar Months

Dr. Burkhard, a specialist in SAPNs nanoparticles will devote effort as needed will help design and produce SAPN-based vaccines as described in this proposal.

Mohammed Bouziane, Ph. D Consortium Scientist 2.0 Calendar Months $35,000

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As Sunomix Therapeutics CEO, Dr. Bouziane will be directly involved in the design, development, cloning, protein expression, purification, refolding, TLR-activation and analysis of SAPN prototype to make them suitable as a platform for COVID 19 vaccine. At least ten prototype that contain different pairs of CD4 and CD8 human epitopes identified from COVID genome in Dr. Benmohamed lab will be produced at Sunomix Therapeutics. All the nanoparticles will contain CpG, the preliminary data using SAPNs produced by Sunomix Therapeutics shows very promising results. Dr. Bouziane will also assist the PI with the in vivo work and data analysis as described in this application. He will supervise a postdoctoral fellow. They will meet weekly to discuss results of SAPNs bio production.

To Be Named Post-Doc-Sr. Scientist 9.0 Calendar Months $55,445
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We need molecular biology Kits and reagents for PCR, cloning, lab consumables to support our in vitro experiments for our various vaccine constructs, as well as gloves, test kits including mycoplasma

and endotoxin, safety supplies and other miscellaneous supplies necessary for a routine functional laboratory.
We are also asking for a yearly budget for the purchase of all of the required plastic ware that is normally used in the laboratory for PCR and molecular biology and virology applications. This includes flasks of all sizes, plates between 6 and 96 wells for PCR, disposable pipettes between 1 and 25 ml volume, barrier tips, and other necessary plastics to carry out the experiments described in the proposal. This category will include other disposable items such as Eppendorf multi-channel tips, and all other liquid handling supplies.

Lab Consumables, Protein Expression, Large scale production of 5 Covid19 SAPNs:
We are requesting a total budget over 1 year duration of: $6,000
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We need bottles of tissue culture medium for scale up production of various vaccine constructs, as well as gloves, SDS-PAGE, test kits, safety supplies, gowns, sterile syringes and needles, and other miscellaneous supplies necessary for a routine functional laboratory. We are also asking for a yearly budget for the purchase of all of the required plastic ware that is normally used in the laboratory for in vitro maintenance of cell cultures and protein expression. This includes flasks of all sizes, disposable pipettes between 1 and 25 ml volume, purification flasks, barrier tips, and other necessary plastics to carry out the experiments described in the proposal. This category will include other disposable items such as Eppendorf multi-channel tips, and all other liquid handling supplies.

Lab Consumables, Protein Purification, Refolding of 5 Covid19 SAPNs:
We are requesting a total budget over 1 year duration of: $9,600
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Purification columns
Lysis, elution buffers
SDS-PAGE.
Protein refolding. For refolding the protein is first rebuffered in specific buffer solution without urea. This quick dilution from denaturing (urea) to native (no urea) buffer conditions triggers refolding of the protein. The solution is then analyzed by negative stain transmission electron microscopy at different resolutions. If needed further screens for optimal refolding conditions can be performed with smaller sampling sizes of the pH and the ionic strength. Additionally, excipients such as trehalose, sucrose, arginine, proline or others can be added, or if needed detergents such as cholate, deoxycholate, tween-80 or others can be added.
TLR-activation. Activation through TLR5 will be assessed for different SAPN prototypes. The testing will be done using TLR/NF-kB/ SEAPorter™ Stably Transfected HEK 293 Stable Cell Lines as follows: All cell lines are stably co-transfected cell lines, which expresses the TLR5 and the secreted alkaline phosphatase (SEAP) reporter gene under the transcriptional control of an NF-kB response element. Using the 96-well plate format assays, TLR/NF-kB/SEAPorter™ HEK 293 cell line are used for screening of compounds as potential TLR5 agonists. The extent of SEAP secreted into the media is indicative of the amount of agonist activity. SEAP catalyzes the hydrolysis of p-Nitrophenyl phosphate (PNPP) producing a yellow product that can be read in a spectrophotometer or ELISA reader at 405 nm. Different concentrations of compounds are used to yield an EC50 value for each compound tested. Positive controls are made using native flagellin. Each compound will be tested in duplicate.

Standard methodology for agonist testing is incubation of compounds in triplicate in 96 well plates at 5X104 cells/well.
Cells are stimulated with control ligand or test compounds at various concentrations. After 24 hour incubation SEAP is analyzed using SEAPorter™ Assay Kit. Dose-responsive percent activation of each sample well will be calculated to yield the ligand EC50 value.
Analysis of the biophysical properties of the SAPNs. The shape and size of the SAPNs will be analyzed using Transmission Electron Microscopy (TEM) and Dynamic Light Scattering (DLS).
Total Direct Cost $114,545.00
Total In direct Cost Fringe benefit (10%) $11,455.00

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals ($)	
Section A, Senior/Key Person		0.00
Section B, Other Personnel		180,890.00
Total Number Other Personnel	4	
Total Salary, Wages and Fringe Benefits (A+B)		180,890.00
Section C, Equipment		
Section D, Travel		
1. Domestic		
2. Foreign		
Section E, Participant/Trainee Support Costs		
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other		
6. Number of Participants/Trainees		
Section F, Other Direct Costs		48,200.00
1. Materials and Supplies	48,200.00	
2. Publication Costs		
3. Consultant Services		
4. ADP/Computer Services		
5. Subawards/Consortium/Contractual Costs		
6. Equipment or Facility Rental/User Fees		
7. Alterations and Renovations		
8. Other 1		
9. Other 2		
10. Other 3		
Section G, Direct Costs (A thru F)		229,090.00
Section H, Indirect Costs		22,910.00
Section I, Total Direct and Indirect Costs (G + H)		252,000.00
Section J, Fee		
Section K, Total Costs and Fee (I + J)		252,000.00

Total Direct Costs less Consortium F&A

NIH policy (NOT-OD-05-004) allows applicants to exclude consortium/contractual F&A costs when determining if an application falls at or beneath any applicable direct cost limit. When a direct cost limit is specified in an FOA, the following table can be used to determine if your application falls within that limit.

Categories	Budget Period 1	Budget Period 2	Budget Period 3	Budget Period 4	Budget Period 5	TOTALS
Total Direct Costs less Consortium F&A	499,999	499,999	499,999	499,999	499,999	**2,499,995**

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

Expiration Date: 03/31/2020

2. *Program Income Section

*Is program income anticipated during the periods for which the grant support is requested?

○ Yes ● No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

*Budget Period *Anticipated Amount ($) *Source(s)

PHS 398 Cover Page Supplement

3. Human Embryonic Stem Cells Section

*Does the proposed project involve human embryonic stem cells? ○ Yes ● No

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, check the box indicating that one from the registry will be used:

Specific stem cell line cannot be referenced at this time. One from the registry will be used.

Cell Line(s) (Example: 0004):

4. Inventions and Patents Section (Renewal applications)

*Inventions and Patents: ○ Yes ○ No

If the answer is "Yes" then please answer the following:

*Previously Reported: ○ Yes ○ No

5. Change of Investigator/Change of Institution Section

❑ Change of Project Director/Principal Investigator

Name of former Project Director/Principal Investigator

Prefix:

*First Name:

Middle Name:

*Last Name:

Suffix:

❑ Change of Grantee Institution

*Name of former institution:

Tracking Number: GRANT13114391 Funding Opportunity Number: PAR-20-178 . Received Date: 2020-05-22T18:02:25.000-04:00

PHS 398 Research Plan

OMB Number: 0925-0001
Expiration Date: 02/28/2023

Introduction	
1. Introduction to Application (for Resubmission and Revision applications)	
Research Plan Section	
2. Specific Aims	SpecificAims1013860960.pdf
3. Research Strategy*	ResaerchStrategy1013860961.pdf
4. Progress Report Publication List	
Other Research Plan Section	
5. Vertebrate Animals	VertebrateAnimals1013860984.pdf
6. Select Agent Research	Biohazards1013860958.pdf
7. Multiple PD/PI Leadership Plan	
8. Consortium/Contractual Arrangements	Consortium_Arrangement1013784344.pdf
9. Letters of Support	LettersOfSupport1013860978.pdf
10. Resource Sharing Plan(s)	ResourceSharingPlan1013784195.pdf
11. Authentication of Key Biological and/or Chemical Resources	AuthenticationOfKeyBiolandChemRes1013784383.pdf
Appendix	
12. Appendix	

Tracking Number: GRANT13114391 Funding Opportunity Number: PAR-20-178. Received Date: 2020-05-22T18:02:25.000-04:00

SPECIFIC AIMS

Developing a Multi-epitope, Pan-Coronavirus Vaccine: Since early January 2020, humanity has been confronting a pandemic caused by the new Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2), which appears to emerge from Wuhan, Hubei Province, China, causing the Coronavirus disease, known today as COVID-19[1-7]. As of May 211th, 2020, COVID-19 outbreak has over 5.1 million confirmed cases worldwide, with 328,061 deaths, prompting the US and WHO authorities to declare a public health emergency[8, 9]. The worst-case scenario is that this emerging COVID-19 outbreak returns and becomes seasonal[10]. **Our long-term goal** is to develop a safe and efficient pan-Coronavirus vaccine to stop/reduce past, current, and future SARS-CoV infections and/or diseases[1]. The majority (80-85%) of newly infected individuals are asymptomatic while a minority of individuals, especially the elderly and those with compromised health, develop a wide range of symptoms and may need a rapid medical intervention to prevent acute respiratory distress syndrome and death[11-16] (**Fig. 1**). While SARS-CoV-2-induced antibody and $CD4^+$ and $CD8^+$ T cell responses are critical in reducing viral infection in the majority of asymptomatic individuals, excessive inflammatory responses and pro-inflammatory cytokine storm lead to immuno-pathology and to acute respiratory distress syndrome in many symptomatic individuals[17]. **Major gaps**: Identifying the epitope specificities and the phenotype and function of the B cells, $CD4^+$ T cells, and $CD8^+$ T cells associated with "natural protection" seen in asymptomatic individuals would inform future safe vaccines to stop or reduce SARS-CoV-2 infection and COVID-19 disease severity (**Figs. 3** and **4**).

Preliminary Data: Over the last 4 months, immediately after the discovery of the first SARS-CoV-2 strain sequence, publicly available in January 10th, 2020[18-22], we have since then made major progress in: (**A**) Identifying *a priori* potential human antibody and $CD4^+$ and $CD8^+$ T cell target epitopes from the whole SARS-CoV-2 genome (**Fig. 4**); (**B**) Identifying "universal" epitopes conserved and common between SARS-CoV-2 and: (1) previous SARS and MERS humans coronaviruses outbreaks[23]; (2) between over 4388 current SARS-CoV-2 strains that now circulate in the United States and 184 other countries; and (3) between bat-derived SARS-like strains[24] (**Fig. 4** and **Table 1**). A "pre-emptive" pan-Coronavirus vaccine targeting the bat-derived SARS-like Coronavirus strains, that may jump into humans in the future, is indispensable in the surveillance of, and preparation to fight, the next Coronavirus outbreak[23, 25-29]; (**C**) [redacted] 6255

Our hypothesis is that at least one of our pan-Coronavirus vaccine candidates, containing conserved "asymptomatic" SARS-CoV-2, B- and T-cell epitopes, which are mainly recognized by the immune system of "protected," asymptomatic individuals will protect from SARS-CoV-2 infection and disease, when delivered intranasally, using our SAPN vaccine delivery platform. To test this hypothesis, we propose two **Specific Aims**: **Aim 1**: To test *in vitro* the antigenicity of conserved Coronavirus epitopes, identified from the whole SARS-CoV-2 genome, using blood-derived antibodies, $CD4^+$ T-cells and $CD8^+$ T-cells from SARS-CoV-2-infected symptomatic vs. asymptomatic individuals. The immunodominant "asymptomatic" epitopes to be used in our multi-epitope pan-Coronavirus vaccine candidates will be identified. **Aim 2**: To test *in vivo* the *safety*, *immunogenicity*, and *protective efficacy* of highly conserved multi-epitope, pan-Coronavirus vaccine candidates, delivered mucosally using our SAPN vaccine delivery platform, into our novel [redacted] 6255 that: (*i*) develops a human-like immune response; (*ii*) is susceptible to SARS-CoV-2 infection; and (*iii*) develops human-like COVID-19 disease including pneumonia, lung histopathology and weight loss[30]. [redacted] . **Outcome**: Successful completion of this preclinical project is expected to identify a broadly protective pan-Coronavirus vaccine candidate which will be moved quickly into an FDA Phase 1 clinical trial.

SIGNIFICANCE

1. ***Unique Characteristics of SARS-CoV-2 virus transmission and potential resurgence of "flu-like" seasonal infection:*** Coronaviruses are a large family of viruses that are common in humans and many different species of animals, including bats, camels and civet-cats[38-43]. There were only two Coronaviruses known to be deadly for humans: the MERS-CoV and SARS-CoV, and both originated from bats and were transmitted from camels and civet-cats, as intermediate animal vectors, to humans, respectively[44-46]. As we are in the midst of an ongoing COVID-19 pandemic caused by a, third deadly Coronavirus, the SARS-CoV-2 that also originated from bats and transmitted to humans from an as-yet-uncertain intermediate animal reservoir, scientists are struggling to understand how SARS-CoV-2 resembles and differs from the other two previously known deadly Coronaviruses, at the genomic and transcriptomic levels, but also at the protective immunity vs. immunopathology collateral damage they induce in humans[47]. Only rarely do animal Coronaviruses infect humans and then spread human-to-human[48]. However, unlike other Coronavirus strains, the new SARS-CoV-2 strain leads to both animal-to-human spread[25] and human-to-human transmission[4, 10, 49-54]. The first known human-to-human transmission of SARS-CoV-2 in the USA was reported in late January 2020[9]. A worst-case scenario is if and when this emerging COVID-19 outbreak transforms into a seasonal infection with no vaccine available [10, 55]. Within 2-14 days after exposure, the newly infected person may develop fever, fatigue, myalgia and respiratory symptoms including cough and shortness of breath[56, 57]. Patients, especially the elderly and those with compromised health, can die rapidly from acute respiratory distress syndrome and multiple organ failure. Mucosal and epithelial tissues are frontline barriers that are continuously exposed to infectious viral pathogens[58-68].

[redacted]

3. *Our self-assembling protein nanoparticles (SAPNs) vaccine delivery system:* A safe and effective prophylactic mucosal vaccine inducing systemic and mucosal anti-viral B- and T-cell immunity against the emergence and rapid expansion of SARS-CoV-2 infection is currently not available[101]. During these last 4 months, we made significant progress in pan-Coronavirus vaccine development, we have identified potential human B-cells, $CD4^+$ T cells, and $CD8^+$ T cells epitopes from SARS-CoV-2 sequences spanning the virus's multi-stage lifecycle. We used the sequences of the first SARS-CoV-2 strain immediately after it became publicly available in early January 2020[82, 102-108]. Using these epitopes, we plan to design up to 16 multi-epitope pan-Coronavirus vaccine candidates using our lab's established methodologies for other viral infections[109-113] [redacted]

[redacted]

4. *Our [redacted] for preclinical testing of human pan-Coronavirus vaccine candidates:* The development of human vaccines for SARS Coronaviruses has been hampered by the lack of a small and reliable [redacted] susceptible to SARS infection mimicking human disease[125-128]. SARS-CoV-2 enters the human body by binding to human ACE2[129-131]. [redacted]

[redacted]
6255

[redacted]
6255

CLINICAL IMPACT

Successful completion of this preclinical vaccine study will have a high medical impact in achieving a breakthrough all-in-one pan-Coronavirus vaccine compound that will induce neutralizing antibodies and $CD4^+$ and $CD8^+$ T cells. Such a "pre-emptive" multi-epitope, pan-Coronavirus vaccine has the potential to protect against not only past and current Coronavirus strains but also against potential future outbreaks. The best pan-Coronavirus vaccine candidate produced by this preclinical study will move to a Phase 1 clinical trial.

INVESTIGATORS

This application gathers a multidisciplinary team of ten top scientists and clinicians who have complementary expertise in different areas of vaccine development. These include: (**1**) The Principal Investigator (Dr. Lbachir BenMohamed, UC Irvine), an immune-virologist and vaccinologist with over 30 years of experience in the area of viral infection/immunity and vaccine development; (**2**) A virologist and a world authority in Coronavirus infections (Dr. Michael Buchmeier, UC Irvine). Dr. Buchmeier brings to the project more than 35 years of experience with the Coronaviruses including SARS-CoV. We expect the daily interaction between Dr. BenMohamed, an immunologist, and Dr. Buchmeier, a Coronavirus expert and an active co-investigator on this vaccine to speed analyzing and correlating the immunological and virological results (both labs are located side-by-side at UC Irvine). Dr. Buchmeier has published a number of seminal discoveries on SARS-CoV infections[146-152]; (**3**) An expert in clinical infectious diseases (Dr. Anthony B. Nesburn, UC Irvine); (**4**) A biostatistician (Dr. Christine McLaren, UC Irvine); (**5**) An expert in inflammation and cytokine storm (Dr. Eric Pearlman, Director, UC Irvine Institute for Immunology); (**6**) An expert in advanced microscopic imaging (Dr. James V. Jester, UC Irvine); (**7**) An expert in SAPNs-based vaccine design and production (Dr. Peter Burkhard, Sunomix Therapeutics, Inc., San Diego). The collaborative project also includes three physicians and clinicians, (**8**) Dr. Donald Forthal; (**9**) Dr. Sebastian Schubl, and (**10**) Dr. Lanny Hsieh all located at UCI's COVID-19 Research Biobank and Biorepository, that help identify COVID-19 patients.

INNOVATION: UNIQUENESS OF OUR PAN-CORONAVIRUS VACCINE STRATEGY

Conceptual innovation: More than 169 vaccines are currently being developed - pre-clinically and clinically - around the world to protect against SARS-CoV-2, using a variety of different approaches[153]. Twelve vaccine candidates are presently in phase I/II clinical trials. **Six major points highlight the novelty and uniqueness of our pan-Coronavirus vaccine compared to other vaccine strategies**:

[redacted]

are distributed in the various human populations[162]. **Technical innovation:**

[redacted]

6255

[redacted]

[redacted]

herpes symptomatic and asymptomatic infection, SARS-CoV-2 infection induces different profile and function of B- and T cell responses in symptomatic vs. asymptomatic patients[83, 171-176].

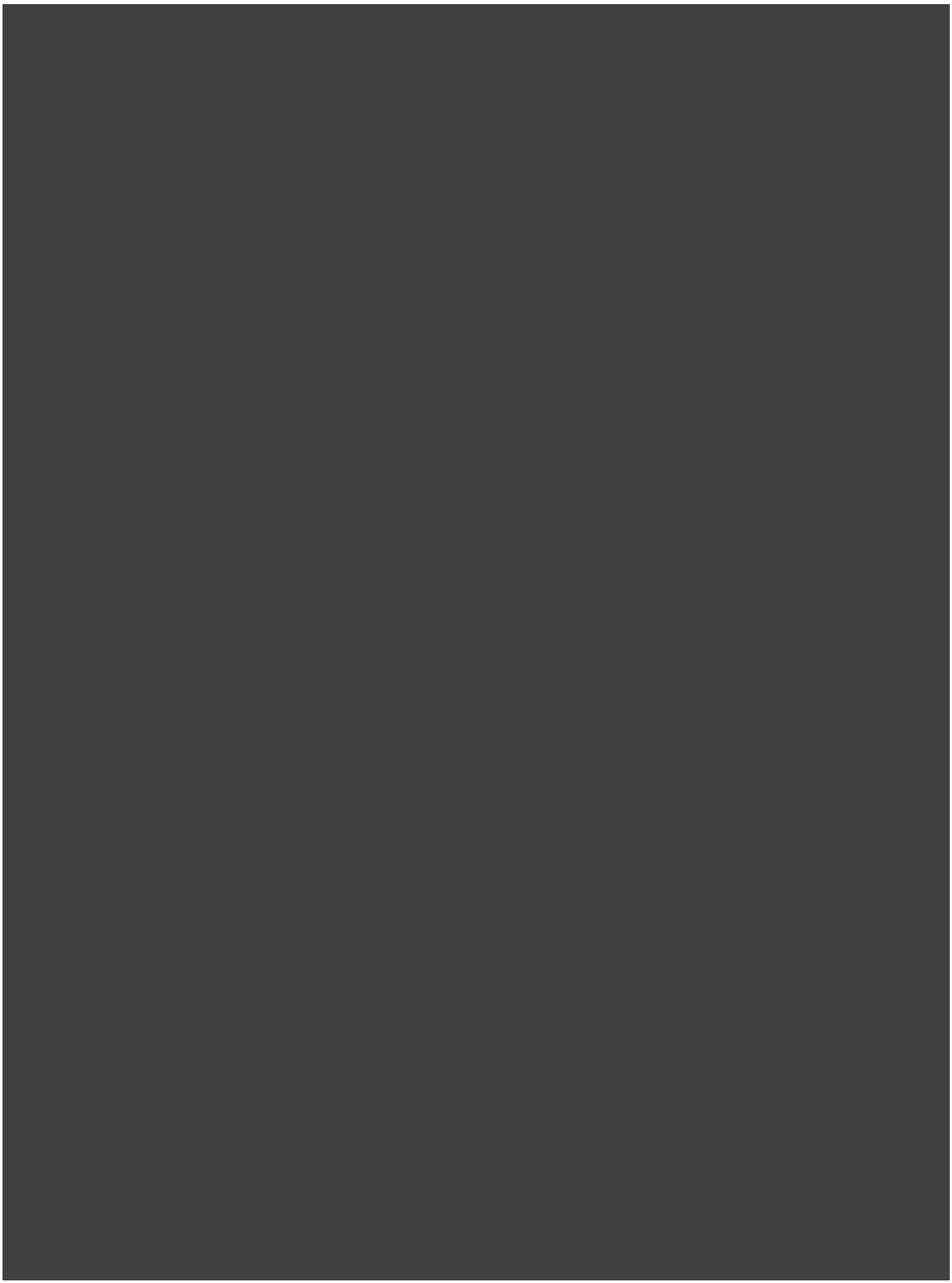
[redacted]

(100%).

[redacted]

[redacted]

[redacted]



hypotheses that not only epitope specificity, but also the nature of T cell responses to SARS-COV-2 epitopes differ in SYMP and ASYMP individuals; and (**d**) most ASYMP memory $CD8^+$ T-cells will be $CD8^+CD62L^{low}CCR7^{low}CD44^{high}$ T_{EM} phenotype. In contrast, most SYMP memory $CD8^+$ T-cells will be of the $CD8^+CD62L^{high}CCR7^{high}CD44^{low}$ T_{CM} phenotype. ***Cytokine storm, T cell function and dysfunction studies***: We do not expect any issues with cytokine assays since we regularly use them in our lab. We expect an increased cytokine storm production, a decreased T cell function and an increase in T cell exhaustion in symptomatic individuals with their $CD8^+$ T-cells will have low proliferation and low cytotoxicity, low levels of IL-2, high IFN-γ, TNF-α, IL-22, IL-17, and MIP-1.

Overall, we expect to identify several "asymptomatic" epitopes that will be selectively recognized by antibodies, $CD4^+$ and $CD8^+$ T-cells derived from SARS-CoV-2-infected but "asymptomatic" individuals. These antigenic "asymptomatic" epitopes will be selected to construct up to 16 multi-epitope pan-Coronavirus vaccine candidates outlined in Aim 2 below. We will leverage on our documented expertise in mapping "asymptomatic" herpes epitopes[109, 110, 112, 113, 182, 183, 203-207] and on our successful preclinical development of an "asymptomatic" epitope-based herpes vaccine[109-113], and expect to similarly identify several of SARS-CoV-2 "asymptomatic" epitopes that will be selectively recognized by antibodies: $CD4^+$ and $CD8^+$ T-cells derived from COVID-19 infected but asymptomatic individuals. In contrast, we expect to identify a handful of "symptomatic" epitopes mainly recognized by "pathogenic" antibodies: $CD4^+$ and $CD8^+$ T-cells derived from symptomatic individuals who develop severe COVID-19.

Potential Pitfalls and **Alternative Approaches:** No technical difficulties are expected since we have previously performed similar immunological experiments in herpes virus SYMP and ASYMP individuals. Our enrolled patient population will have enough SYMP and ASYMP individuals to provide more than 90% power for statistical analyses, as we previously described[184, 206, 208-211]. Alternatively, we may not detect differences in the nature or magnitude of T-cell responses in SARS-CoV-2-infected SYMP vs. ASYMP patients, suggesting that our hypothesis is incorrect. Although very unlikely, if future screenings fail to define discrete "SYMP" and "ASYMP" T cell epitopes as we expect, we will still be able to identify immunodominant SARS-CoV-2 epitopes and study their immunogenicity and protective efficacy in our susceptible HLA-DR/HLA-A*0201/hACE2 triple 6255 model, as detailed in Aim 2. In addition, we will determine whether asymptomatic individuals have predominant $CD4^+$ and $CD8^+$ T cells that will produce IL-17A, IL-22, and TGFβ1. In the very unlikely event that we cannot identify "asymptomatic" human B and T cell epitopes from Aim 1; in Aim 2 we will still proceed with pan-Coronavirus vaccine candidates that would incorporate immunodominant and conserved B and T cell epitopes. These epitopes would be highly recognized by antibodies and T cells from SARS-CoV-2 seropositive individuals. Therefore, the success of Aim 2 does not depend on the success of Aim 1.

Specific Aim 2: To test *in vivo* the *safety*, *immunogenicity*, and *protective efficacy* of highly conserved multi-epitope pan-Coronavirus vaccine candidates delivered mucosally using a novel "humanized" and susceptible 6255 model.

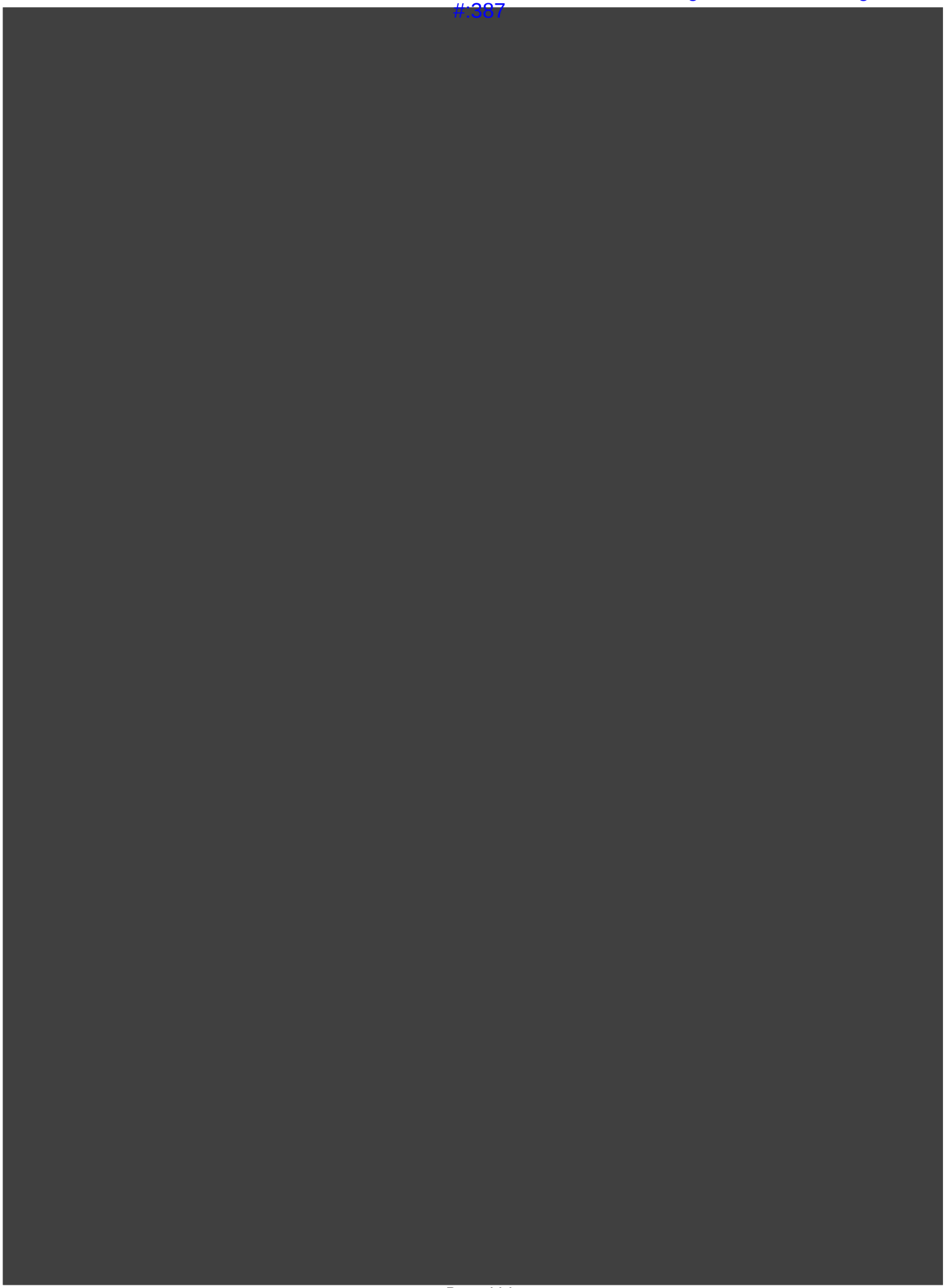
We hypothesize that a multi-epitope pan-Coronavirus vaccine that exclusively incorporates "asymptomatic" SARS-CoV-2-derived B- and T-cell epitopes (**Fig. 7**), delivered using SAPN nanoparticles platform (**Fig. 2**), should protect against SARS-CoV infection and disease. **End point**: Up to 16 pan-Coronavirus vaccine candidates will be test and the best pan-Coronavirus vaccine candidate that induce better protective immunity against SARS-CoV, SARS-CoV-2, and Bat SARS-CoV-like

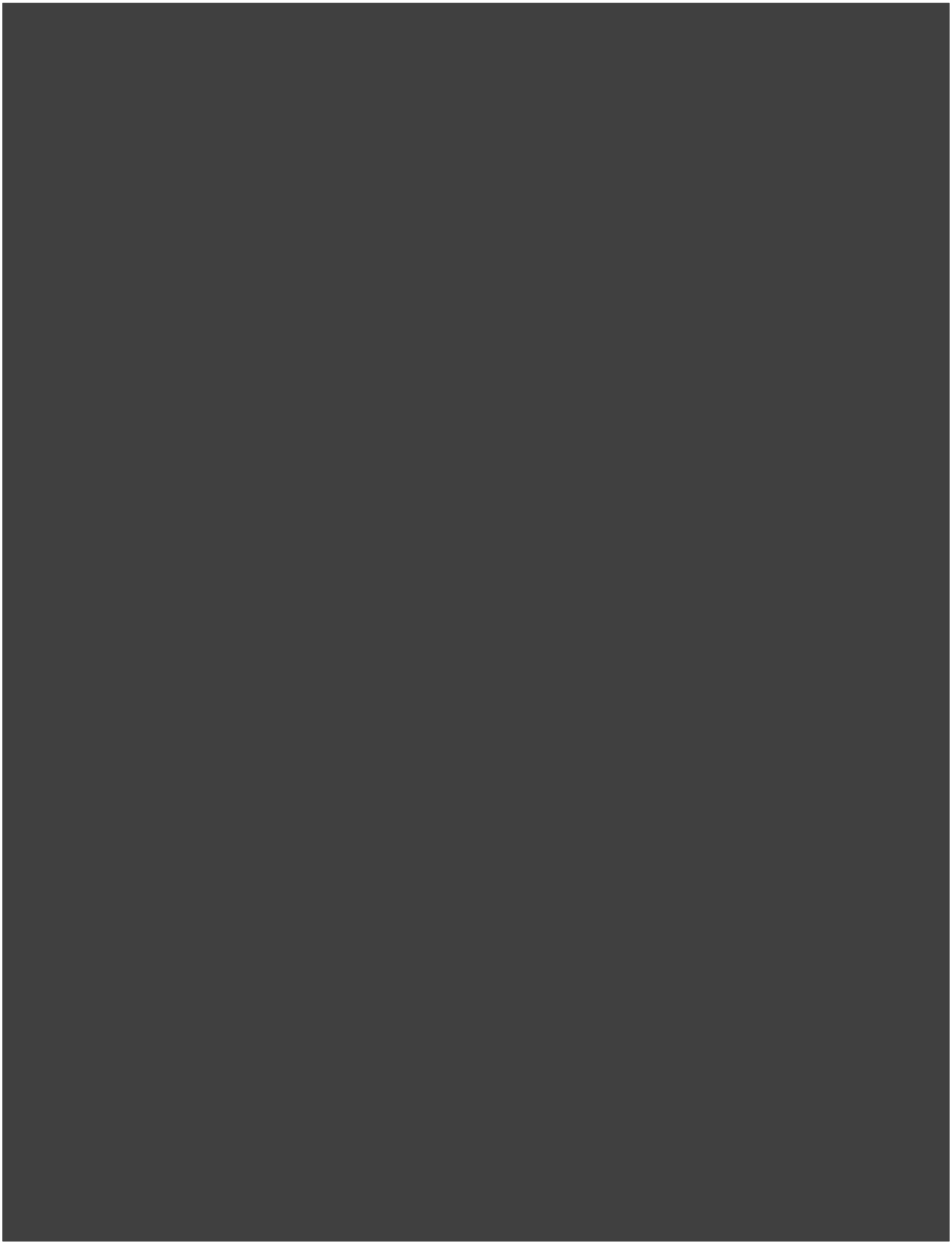
infections and disease in vaccinated and infected transgenic mice will be selected for clinical trial.

Experimental Design: In Aim 2, we leverage our multi-epitope SAPN-based vaccine design approaches for a herpes virus vaccine and extend it to COVID-19. We will design, produce and pre-clinically test 16 pan-Coronavirus vaccine candidates that incorporate highly conserved and potentially protective 'asymptomatic" B- and T-cell epitopes identified from SARS-CoV-2[126-128]. The *safety*, *immunogenicity* and *protective efficacy* of 16 multi-epitope, pan-Coronavirus vaccine candidates will be tested *in vivo* (**Fig. 6**), using our established self-adjuvant SAPN-based vaccine (**Fig. 2**) delivered *in vivo* in our novel "humanized" susceptible [redacted] that: (*i*) develops a human-like immune response; (*ii*) is susceptible to SARS-CoV-2 infection; and (*iii*) develop human-like COVID-19 disease[30]. We will: (**a**) produce and test up to 16 SAPN-based PanCoV vaccine candidates that incorporate target "asymptomatic" B-cell, $CD4^+$ and $CD8^+$ T-cell epitopes identified in Aim 1; (**b**) deliver these pan-Coronavirus vaccine candidates using our established SAPN vaccine delivery platform already tested and proven in our lab[109, 157, 158]; (**c**) test three different immunization routes: (*i*) intranasal route; (*ii*) sub-lingual route; and (*iii*) topical ocular route; and (**d**) test the durability of protection and its correlation with blocking/neutralizing antibodies and the number/function of tissue-resident SARS-Cov-2-specific $CD4^+$ and $CD8^+$ T_{RM} cells in the [redacted]

Construction of SAPNs-based pan-Coronavirus vaccine candidates incorporating SARS-Cov-2 B- $CD4^+$ T cell and $CD8^+$ T cell epitopes: As illustrated in **Fig. 4**, we have made significant progress: In identifying from the whole SARS-CoV-2 genome *a priori* potential and highly conserved human B-cell and $CD4^+$ and $CD8^+$ T cell target epitopes. These human-conserved epitopes, that are antigenic in asymptomatic humans (Aim 1) and immunogenic in [redacted] (Aim 2), will be incorporated in our multi-epitope pan-Coronavirus vaccine candidates (**Fig. 7**). **Various Combination of B, $CD4^+$ and $CD8^+$ T cells epitopes**: Based on the epitopes selected in Aim 1 will be constructed. Combinations of peptide epitopes selected in Aim 1 will be delivered with CpG and Flagellin adjuvant in HLA-A*0201, HLA-DRB1*0101 and HLA-DRB1*0104 mice to determine the most robust combinations that elicit neutralizing Abs, cytotoxicity and cytokine production. The most immunogenic combinations of B, $CD4^+$ and $CD8^+$ T cells epitopes will then be used to construct multi-epitope pan-Coronavirus vaccines. Based on (**1**) the number of B, $CD4^+$ and $CD8^+$ T cell highly

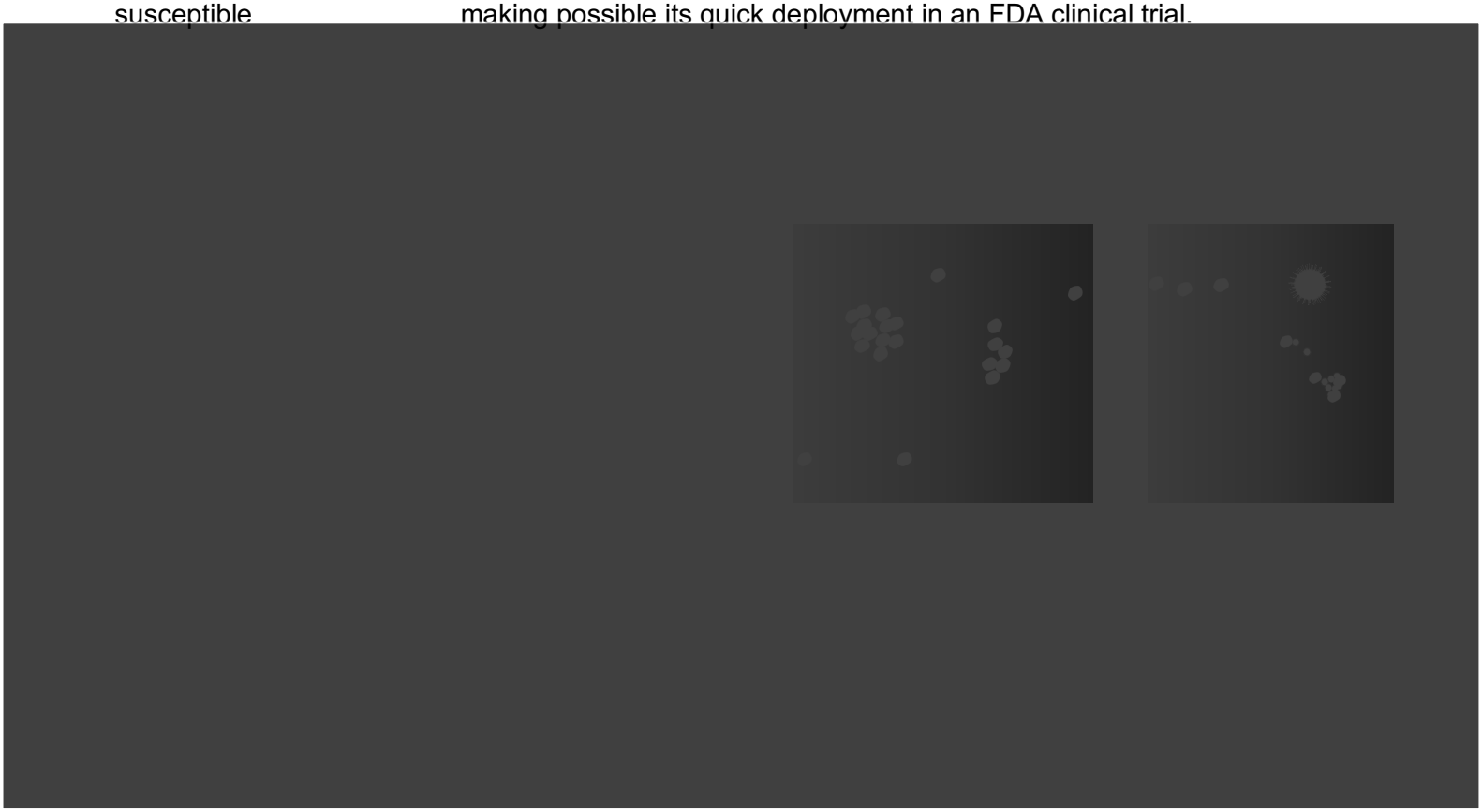
[redacted]





SAFETY OF THE PAN-CORONAVIRUS VACCINE

Unlike past Coronavirus vaccines that showed pathogenicity[232-235], we expect our SAPN-based pan-Coronavirus vaccine candidates to be safe since they incorporate only "asymptomatic" epitopes. The nanoparticle SAPN-based antigen delivery platform, used to deliver our Coronavirus vaccines, have already shown safety in Phase I/IIa clinical trials for other pathogens[114-124]. It is likely that our multi-epitope pan Coronavirus vaccine will protect from SARS-CoV-2 infection and COVID-like disease in our susceptible making possible its quick deployment in an FDA clinical trial.



Timetable: **Year 1:** *Begin in vitro* human studies in Aim 1, begin Aim 2, *in vivo* studies for pan-CoV vaccine candidates #1 to #5. **Year 2:** Complete Aim 1, and complete studies on pan-CoV vaccine candidates #1 to #5 and begin pan-CoV vaccine candidates #6 to #10. **Year 3:** Complete studies on pan-CoV vaccine candidates #6 to #10 and begin pan-CoV vaccine candidates #11 to #16. **Year 4:** Complete immunology and virology studies for pan-CoV vaccine candidates #1 to #16. **Year 5:** Complete analyzing $CD4^+$ and $CD8^+$ T cells cell depletion and transfer and complete selection of the final best safe, immunogenic and protective pan-Coronavirus vaccine candidate for a phase 1 clinical trial.

PHS Human Subjects and Clinical Trials Information

OMB Number: 0925-0001 and 0925-0002

Expiration Date: 03/31/2020

Are Human Subjects Involved	● Yes ○ No
Is the Project Exempt from Federal regulations?	● Yes ○ No
Exemption Number	☐ 1 ☐ 2 ☐ 3 ☑ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8
Other Requested Information	

Human Subject Studies

Study#	Study Title	Clinical Trial?
1	Developing a Multi-epitope Pan-Coronavirus Vaccine	No

Section 1 - Basic Information (Study 1)

OMB Number: 0925-0001 and 0925-0002
Expiration Date: 03/31/2020

1.1. Study Title *

Developing a Multi-epitope Pan-Coronavirus Vaccine

1.2. Is this study exempt from Federal Regulations * ● Yes ○ No

1.3. Exemption Number ☐ 1 ☐ 2 ☐ 3 ☑ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8

1.4. Clinical Trial Questionnaire *

1.4.a. Does the study involve human participants?	● Yes	○ No
1.4.b. Are the participants prospectively assigned to an intervention?	○ Yes	● No
1.4.c. Is the study designed to evaluate the effect of the intervention on the participants?	○ Yes	● No
1.4.d. Is the effect that will be evaluated a health-related biomedical or behavioral outcome?	○ Yes	● No

1.5. Provide the ClinicalTrials.gov Identifier (e.g. NCT87654321) for this trial, if applicable

Section 2 - Study Population Characteristics (Study 1)

2.1. Conditions or Focus of Study

- The goal of this mechanistic and translational project is to determine the mechanisms that led to antibodies, CD4+ and CD8+ T cells function and exhaustion seen in SARS-CoV infection and disease in humans.

2.2. Eligibility Criteria

We will use COVID-19 “symptomatic” and “asymptomatic” (never had any disease) men and women patients.

2.3. Age Limits	Min Age: 18 Years	Max Age:	63 Years
2.4. Inclusion of Women, Minorities, and Children	InclusionOfWomenandMinorChildren1013784403.pdf		
2.5. Recruitment and Retention Plan	RecruitmentandRetentionPlan1013784395.pdf		
2.6. Recruitment Status	Active, not recruiting		
2.7. Study Timeline	StudyTimeline1013784396.pdf		
2.8. Enrollment of First Subject	09/01/2020	Anticipated	

INCLUSION OF WOMEN, MINORITIES, AND CHILDREN

Women and Minorities are included in this application. Children are not included in this application.

RECRUITMENT AND RETENTION PLAN

Symptomatic and Asymptomatic patients: During the last 5 weeks (i.e., January to May 2018), we have screened individuals for SARS-CoV seropositivity. Among these, we will enrolled 50 immuno-competent individuals who were seropositive for SARS-CoV. The subjects were White, African, Asian, Hispanic, and other minor ethnicities, with an age range of 18-65 (median 32): 50% were females, and 50% were males. All patients were negative for HIV and HBV, and had no history of immunodeficiency. All patients were HLAA*0201 positive (corresponding to the type of [redacted] used in this proposal). This haplotype is highly represented as it covers over 50% of the human population, regardless of ethnicity. 50 patients will be asymptomatic (never had any COVID-19 disease based on their self-report and on physician examination). The other 50 patients suffered severe lung lesions and were defined as symptomatic. To investigate reactivated SARS-CoV shedding, nasal swabs will be taken. Asymptomatic vs. symptomatic represent the two extreme situations: Since the spectrum of COVID-19 disease is wide, it would be difficult to assign a subset of B-cells,$CD4^+$ or CD8+ T cells to a specific COVID-19 disease type. Thus, for simplicity, we use just the extreme populations: “symptomatic” (severe COVID-19 symptoms) and “asymptomatic” (SARS-CoV infected but never had any COVID disease). 50 healthy control individuals were seronegative for SARS-CoV and had no history of COVID disease. A history of SARS-CoV infections and usage of any antiviral and anti-inflammatory medication was taken and 40-100-mL blood was collected and used either fresh or frozen. Sera were tested for SARS-CoV using PCR and ELISA Kits and serotyping was confirmed by western blot. Patients were excluded if they were pregnant or breastfeeding.

STUDY TIMELINE

During first 5 months, symptomatic and asymptomatic COVID-19 patients are being screened and recruited at our COVID Bio Bank at UC Irvine. 6 to 24-months study of immune responses in symptomatic and asymptomatic COVID patients will be performed in this study. We will follow up some symptomatic and asymptomatic patients approximately 3 years. We will perform data analysis and report results during the last 2 years of the project.

Inclusion Enrollment Reports

IER ID#	Enrollment Location Type	Enrollment Location
Study 1, IER 1	Domestic	UCI Medical Center

Inclusion Enrollment Report 1

Using an Existing Dataset or Resource* : ❍ Yes ● No

Enrollment Location Type* : ● Domestic ❍ Foreign

Enrollment Country(ies): USA: UNITED STATES

Enrollment Location(s): UCI Medical Center

Comments: Age [median (range) year]: 31 (18-63)
SARS-CoV status [N (%)]:
SARS-CoV-seropositive 100 (75)
SARS-CoV-seronegative 50 (50)
COVID disease status [N (%)]:
Seropositive Symptomatic 50 (50)
Seropositive Asymptomatic 50 (50)

Planned

Racial Categories	Ethnic Categories				Total
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/ Alaska Native	2	3	0	0	5
Asian	14	13	0	0	27
Native Hawaiian or Other Pacific Islander	2	3	0	0	5
Black or African American	14	13	0	0	27
White	43	43	0	0	86
More than One Race	0	0	0	0	0
Total	75	75	0	0	150

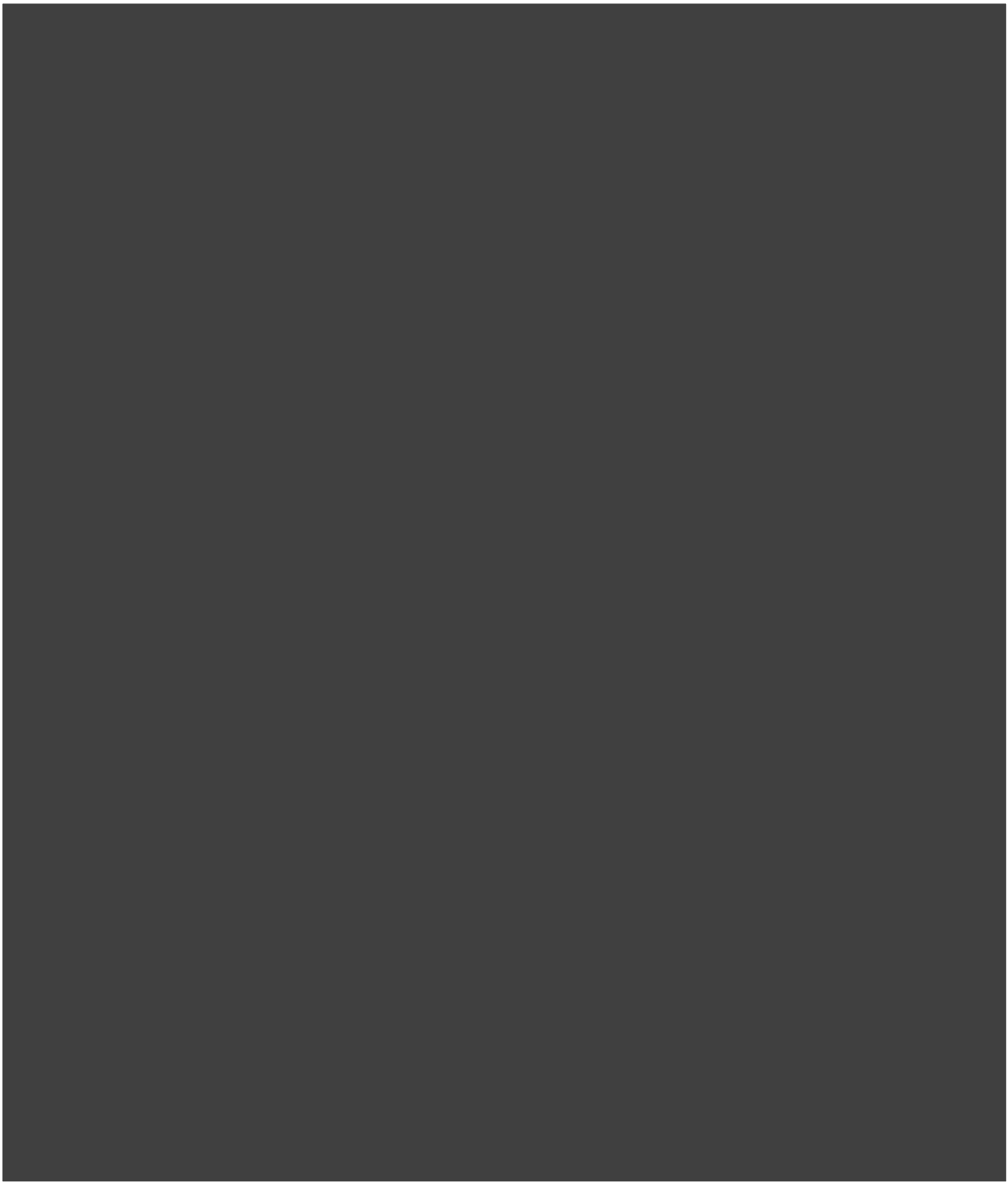
Cumulative (Actual)

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/ Alaska Native	0	0	0	0	0	0	0	0	0	0
Asian	0	0	0	0	0	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	0
Black or African American	0	0	0	0	0	0	0	0	0	0
White	0	0	0	0	0	0	0	0	0	0
More than One Race	0	0	0	0	0	0	0	0	0	0
Unknown or Not Reported	0	0	0	0	0	0	0	0	0	0
Total	0	0	0	0	0	0	0	0	0	0

Section 3 - Protection and Monitoring Plans (Study 1)

3.1. Protection of Human Subjects	ProtectionOfHumanSubjects1013860985.pdf
3.2. Is this a multi-site study that will use the same protocol to conduct non-exempt human subjects research at more than one domestic site?	❍ Yes ● No ❍ N/A
If yes, describe the single IRB plan	
3.3. Data and Safety Monitoring Plan	
3.4. Will a Data and Safety Monitoring Board be appointed for this study?	❍ Yes ● No
3.5. Overall structure of the study team	

PROTECTION OF HUMAN SUBJECTS



Section 4 - Protocol Synopsis (Study 1)

4.1. Brief Summary

4.2. Study Design

4.2.a. Narrative Study Description

4.2.b. Primary Purpose

4.2.c. Interventions

Type	Name	Description

4.2.d. Study Phase

Is this an NIH-defined Phase III Clinical Trial? ❍ Yes ❍ No

4.2.e. Intervention Model

4.2.f. Masking ❍ Yes ❍ No

❑ Participant ❑ Care Provider ❑ Investigator ❑ Outcomes Assessor

4.2.g. Allocation

4.3. Outcome Measures

Type	Name	Time Frame	Brief Description

4.4. Statistical Design and Power

4.5. Subject Participation Duration

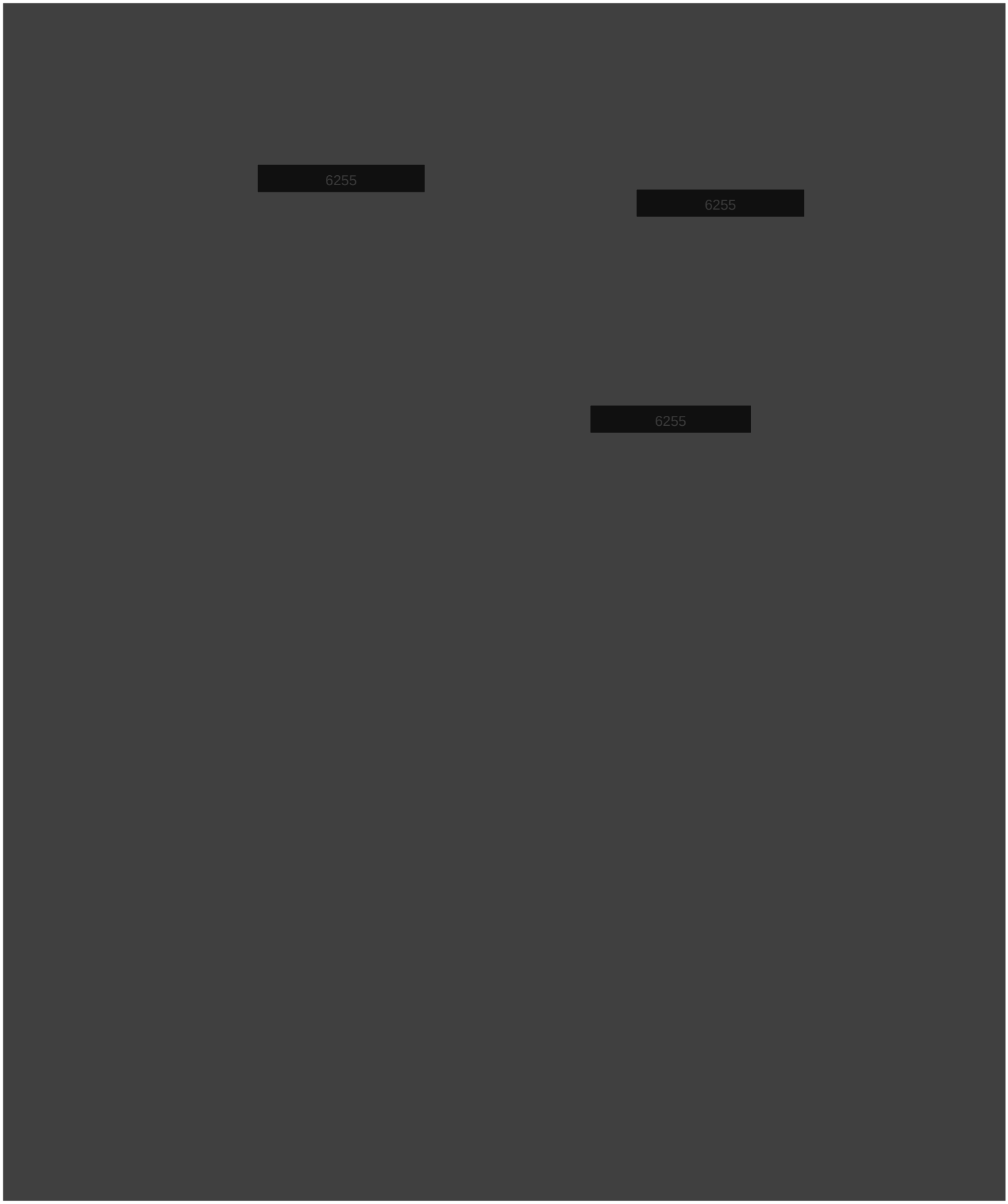
4.6. Will the study use an FDA-regulated intervention? ❍ Yes ❍ No

4.6.a. If yes, describe the availability of Investigational Product (IP) and Investigational New Drug (IND)/ Investigational Device Exemption (IDE) status

4.7. Dissemination Plan

Delayed Onset Studies

Delayed Onset Study#	Study Title	Anticipated Clinical Trial?	Justification
The form does not have any delayed onset studies			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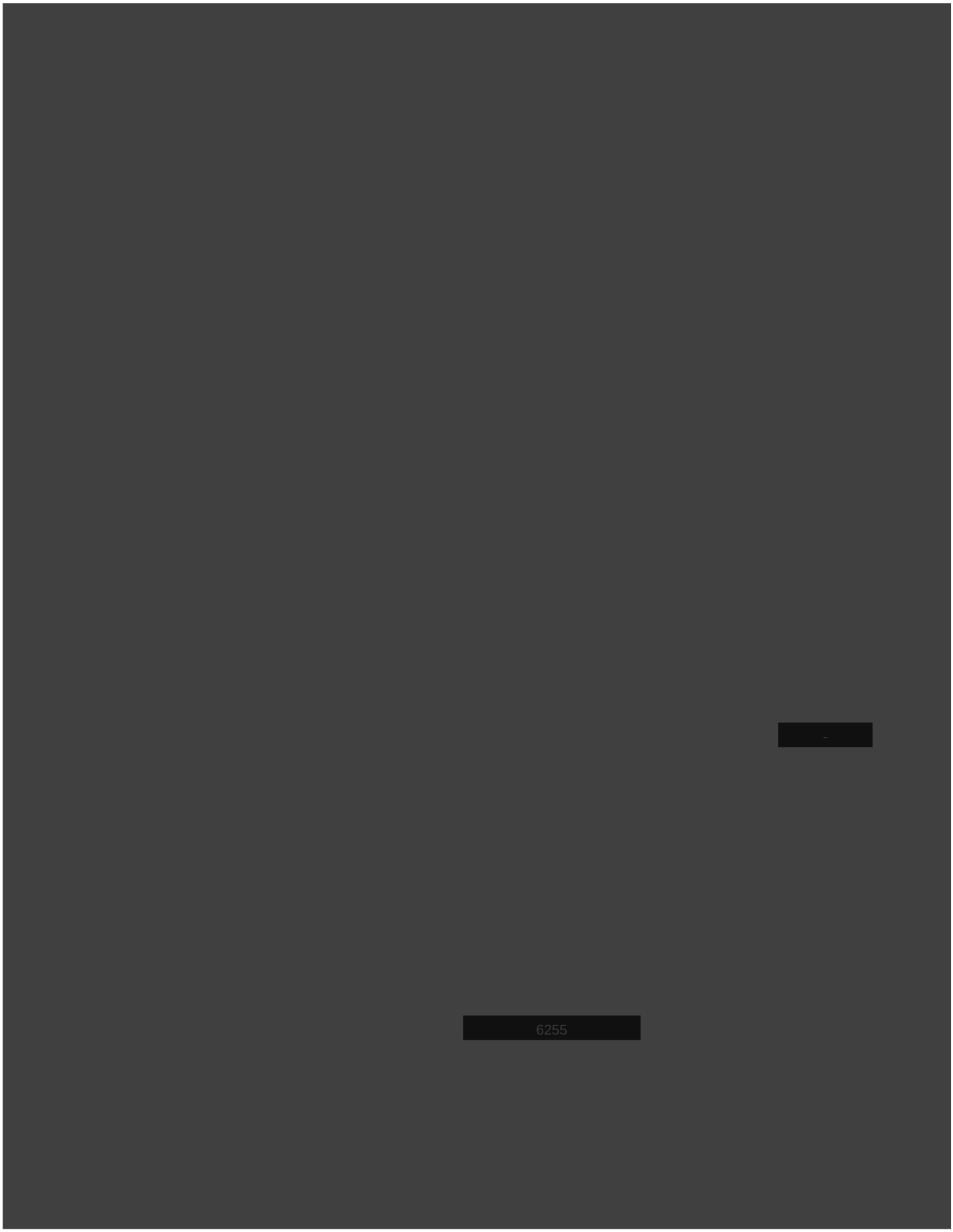
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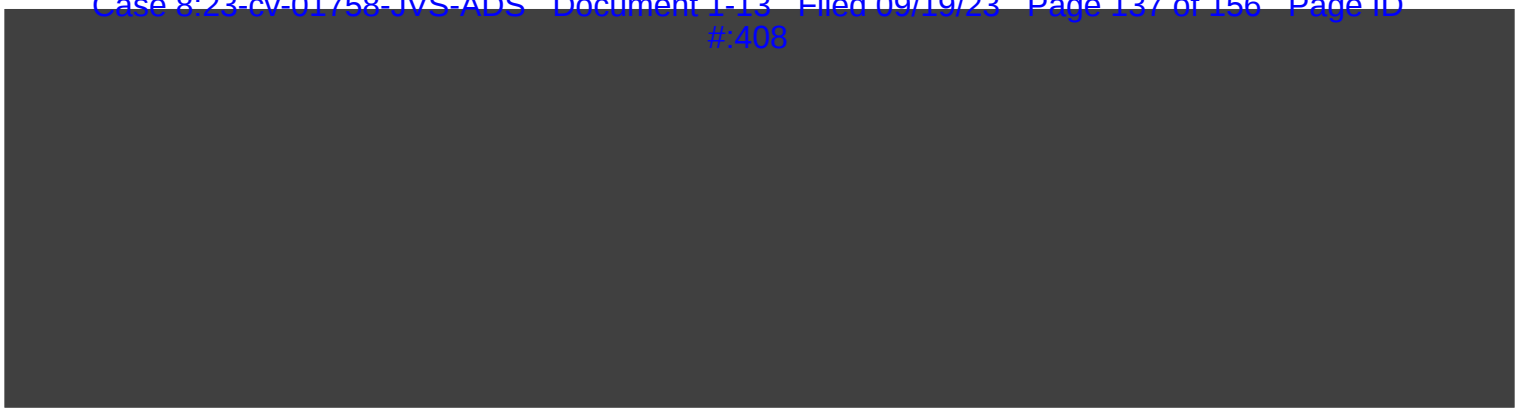

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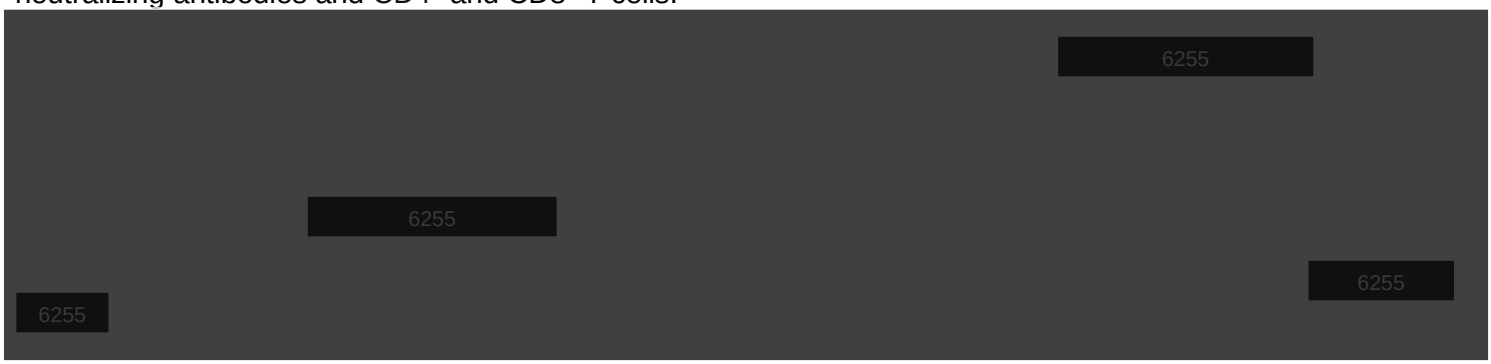
CONSORTIUM ARRANGEMENT

The scope of work of this R01 grant entitled "**Developing a Multi-epitope Pan-Coronavirus Vaccine**" is to develop a Self-Assembling Protein Nanoparticles (SAPNs) vaccine against COVID -19 that will induce robust antibodies local CD4+ and CD8+ T cell responses. Humanity has been confronting a pandemic caused by the new Corona Virus 2 (SARS-CoV-2) infection. **Our long-term goal** is to develop a potent pan-Coronavirus vaccine to stop/reduce past, current and future Coronavirus infections and/or diseases. Coronaviruses present a significant threat due to their high mortality and lack of FDA-approved drugs or vaccines, with new variants that could still be emerging. Successful completion of this preclinical vaccine study will have a high medical impact in achieving a breakthrough all-in-one pan-Coronavirus vaccine construct that will induce protective neutralizing antibodies and $CD4^+$ and $CD8^+$ T cells.



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Please reply to:

DEPARTMENT OF MEDICINE
UCI SCHOOL OF MEDICINE

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May 7th, 2020

Dr. Lbachir BenMohamed, PhD.
Professor & Director
Cellular & Molecular Immunology Laboratory
Gavin S. Herbert Institute
UC Irvine, School of Medicine

Dear Lbachir,

I am writing to confirm my enthusiastic support and collaboration for your new R01 grant proposal entitled "*Developing a Multi-epitope, Pan-Coronavirus Vaccine"* to be submitted to the National Institute of Allergy and Infectious Diseases.

Your proposed novel prophylactic pan-Coronavirus vaccine strategy that uses selected highly conserved and "asymptomatic" epitopes would constitute a paradigm shift in the COVID-19 clinical vaccine field, which has focused on using whole proteins or whole viruses.

As Professor and Director of Biostatistics, Department of Medicine, UC Irvine, I will work to ensure that appropriate statistical expertise is available for this vaccine research project, including advice on study design and analysis of your research data.

It was a pleasure to collaborate with you on the study design of this proposal and I look forward to our continued collaboration.

Yours Sincerely,

Christine E. McLaren

Christine E. McLaren, Ph.D.
Professor, Department of Medicine
Director of Biostatistics

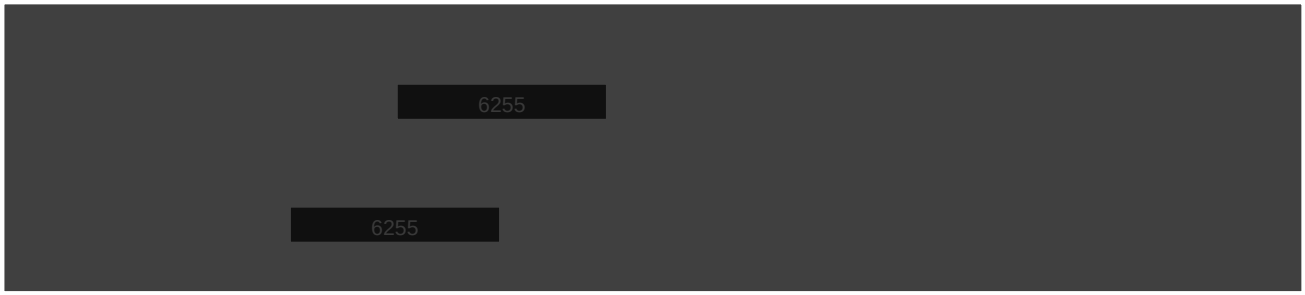
INSTITUTE FOR IMMUNOLOGY
UNIVERSITY of CALIFORNIA, IRVINE

May 14, 2020

Lbachir BenMohamed, PhD
Professor & Director
Cellular & Molecular Immunology Laboratory
Gavin S. Herbert Institute
University of California, Irvine

Dear Lbachir,

I am very much looking forward to work with you on your new vaccine project entitled: "*Developing a Pan-Coronavirus Vaccine"*. My experience on the host inflammatory response to infectious diseases and the fact that our labs are adjacent to each other's will continue to facilitate our collaboration. Our collaboration is also clear from a recent co-authored paper in Frontiers in Immunology on inflammasome activation in herpes simplex corneal infection (keratitis).



Your preliminary results identifying "asymptomatic" SARS-CoV human epitopes will complement the exciting results you obtained recently on the phenotype and function of $CD4^+$ T cells and $CD8^+$ T cells in SARS-CoV infected individuals. I think the use of the [redacted] 6255 model to examine your innovative *Prime/Pull Pan-Coronavirus Vaccine* outlined in your proposal will also contribute to our understanding of the role of $CD4^+$ T cells and $CD8^+$ T cells in protection against COVID-19.

In addition to our proposed collaborations, as the Director of Institute of Immunology, I have established a Flow Cytometry Core that includes a state of the art FACS-ARIA fusion system for flow cytometry and sorting, and an Amnis ImageStream X for imaging individual cells, all of which your research group has full access to.

Wishing you the best of luck with this application,

Sincerely,

Eric Pearlman, PhD
Director, Institute of Immunology
Professor, Departments of Ophthalmology, and Physiology and Biophysics
University of California, Irvine
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April 15th, 2020

Lbachir BenMohamed, PhD
Professor/Director
University of California Irvine

Dear Lbachir,

I am very excited at the prospect of investigating the new vaccine strategy **"Developing a Pan-Coronavirus Vaccine"** described in your new R01 grant proposal to the NIH.

The new prime/pull vaccine strategy proposed in this new R01 vaccine project is expected to induce more tissue resident SARS-CoV-specific $CD4^+$ and $CD8^+$ T cells in lungs and brain.

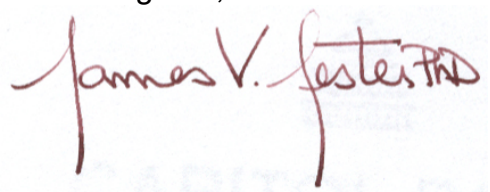
Your proposal, which bridges contemporary virology and immunology is innovative.

We will employ intracellular immunohistochemistry to identify $CD4^+$ and $CD8^+$ T cells within frozen sections of infected and uninfected lung mucosa and brain tissues for surface staining for leukocyte population markers.

We will also use several in lungs and brain sections (~2um each) and a novel Multiplexed High-Resolution Macroscopy technique for 3D reconstruction of in lungs and brain sections. This will allow us to determine co-localization of SARS-CoV-infected neurons with $CD4^+$ and $CD8^+$ T cells three-dimensionally in and at high-resolution on a macroscopic scale.

I look forward to a fruitful collaboration on this exciting project

Warm Regards,



James V. Jester, Ph.D.
Jack H. Skirball Endowed Research Chair
Professor of Ophthalmology and Biomedical Engineering

RESOURCE SHARING PLAN

Sharing Model Organisms: Research Resources generated with funds from this grant will be freely distributed upon request to qualified academic investigators for non-commercial research, to the extent that third-party patent rights and agreements permit and subject to availability.

[redacted]

Antigen Discovery Inc. will adhere to the NIH Grants Policy on Sharing of Unique Research Resources including the “Sharing of Biomedical Research Resources: Principles and Guidelines for Recipients of NIH Grants and Contracts”, issued in December, 1999.

Specifically, material transfers to non-profit researchers would be made with no more restrictive terms than in the Simple Letter Agreements or the Uniform Biological Material Transfer Agreement (UBMTA) and without research through requirements to the extent permitted by any third-party patent or contract obligations. Should any intellectual property arise which Antigen Discovery Inc. decides to patent, we would ensure that the technology remains widely available to the non-profit research community in accordance with the NIH Principles and Guidelines.

The investigators have previously published their data in numerous publications and presented at worldwide scientific meetings, and it is their intention to continue to share data at the earliest opportunities throughout this research project. In particular: Results will be written up and sent for publication in relevant journals. The PI will seek to present publishable results at scientific conferences.

In accordance with NIH Data Sharing Policy, we will look to share data at the earliest opportunities throughout this research project, subject to intellectual property aspects.

Genome Wide Association Studies: Not applicable.

AUTHENTICATION OF KEY BIOLOGICAL AND CHEMICAL RESOURCES